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The Earlier The Better:
The New Frontiers of Lipid Research for Cardiovascular Disease Prevention

034
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FOCUS: United by Unique: Honoring Every Story on World Cancer Day 2026

Optimizing the Therapeutic Landscape in Managing Dyslipidemia – A Discussion on the 2025 Update of the 2019 ESC/EAS Guidelines

Uncovering the Role of Zanubrutinib in Countering Follicular Lymphoma

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Atozet®
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Strike Strong *with* Confidence on LDL-C

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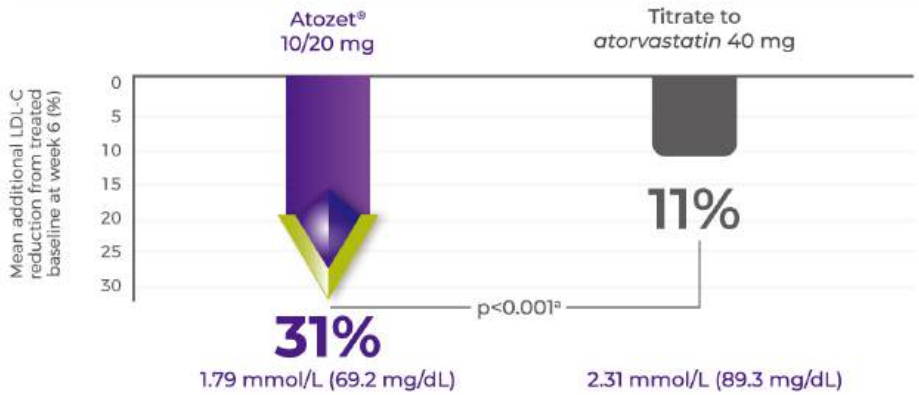
In a clinical study of moderately high-risk patients with hypercholesterolemia on atorvastatin 20 mg who were randomized to receive either Atozet® 10/20 mg or atorvastatin 40 mg[1]

From *atorvastatin* 20 mg



- Mean treated baseline LDL-C for patients receiving Atozet® 10/20 mg (n=92) was 3.10 mmol/L (119.9 mg/dL) and 3.05 mmol/L (117.9 mg/dL) for those titrated to atovastatin 40 mg (n=92).
- **Target:** Patients with hypercholesterolemia at moderately high risk of CHD to achieve LDL-C <2.6 mmol/L (100 mg/dL).

Atozet® 10/20 mg provided superior LDL-C lowering efficacy versus doubling the dose of atorvastatin 20 mg

Prescribe Atozet® for moderately high-risk hypercholesterolemia patients with coronary heart disease who require LDL-C reduction beyond what statin alone can achieve.

LDL-C = Low-density lipoprotein cholesterol

Study design: The TEMPO study was an international, multicenter, double-blind, randomized, parallel-group, titration 6-week study, including 196 patients. The study was designed to evaluate the efficacy and safety profile of Atozet® 10/20 mg compared with doubling atorvastatin to 40 mg/day in patients with hypercholesterolemia at moderate risk of CHD who did not reach LDL-C goal <2.6 mmol/L (<100.5 mg/dL) with atorvastatin 20 mg. Patients receiving atorvastatin 20 mg with LDL-C 2.6 mmol/L (100.5 mg/dL) and 4.13 mmol/L (159.7 mg/dL) were randomized to receive Atozet® 10/20 mg or atorvastatin 40 mg. The primary endpoint was the mean percentage change from baseline LDL-C. Secondary endpoints included percentage of patients achieving LDL-C <2.6 mmol/L (<100.5 mg/dL) and the percentage change from baseline to 6 weeks in TC, TG, HDL-C, non-HDL-C, apo B and high-sensitivity C-reactive protein.

Reference: 1. Conard, S.E. et al. Efficacy and safety of ezetimibe added on to atorvastatin (20 mg) versus uptitration of atorvastatin (to 40 mg) in hypercholesterolemic patients at moderately high risk for coronary heart disease. American Journal of Cardiology. 2008;102(11):1489-1494.

Selected Safety Information of ATOZET®: Indications: Prevention of Cardiovascular Events: ATOZET is indicated to reduce the risk of cardiovascular events in patients with coronary heart disease (CHD) and a history of acute coronary syndrome (ACS), either previously treated with a statin or not. HYPERCHOLESTEROLAEMIA: ATOZET is indicated as adjunctive therapy to diet for use in adults with primary (heterozygous familial and non-familial) hypercholesterolaemia or mixed hyperlipidaemia where use of a combination product is appropriate - patients not appropriately controlled with a statin alone - patients already treated with a statin and ezetimibe. HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLAEMIA (HOFH): ATOZET is indicated as adjunctive therapy to diet for use in adults with HoFH. Patients may also receive adjunctive treatments (e.g., low-density lipoprotein [LDL] apheresis). CONTRAINDICATIONS: - Hypersensitivity to the active substances or to any of the excipients. - Therapy with ATOZET is contraindicated during pregnancy and breast-feeding, and in women of child-bearing potential not using appropriate contraceptive measures. - ATOZET is contraindicated in patients with active liver disease or unexplained persistent elevations in serum transaminases exceeding 3 times the upper limit of normal (ULN). - ATOZET is contraindicated in patients treated with the hepatitis C antivirals glecaprevir/pibrentasvir. PRECAUTIONS: Myopathy/Rhabdomyolysis: In post-marketing experience with ezetimibe, cases of myopathy and rhabdomyolysis have been reported. Most patients who developed rhabdomyolysis were taking a statin concomitantly with ezetimibe. Rhabdomyolysis has been reported very rarely with ezetimibe monotherapy. Also, ATOZET contains atorvastatin, which is a HMG-CoA reductase inhibitor. Atorvastatin may in rare occasions affect the skeletal muscle and cause myalgia, myositis, and myopathy that may progress to rhabdomyolysis. A CPK level should be measured before starting treatment. If CPK levels are significantly elevated (>5 times ULN) at baseline, treatment should not be started. Patients must be asked to promptly report muscle pain, cramps, or weakness especially if accompanied by malaise or fever or if muscle signs and symptoms persist after discontinuing ATOZET. Liver Enzymes: Liver function tests should be performed before the initiation of treatment and periodically thereafter. Should an increase in transaminases of greater than 3 times the ULN persist, reduction of dose or withdrawal of ATOZET is recommended. Hepatic Insufficiency: Due to the unknown effects of the increased exposure to ezetimibe in patients with moderate or severe hepatic insufficiency, ATOZET is not recommended. Interstitial lung disease: If it is suspected a patient has developed interstitial lung disease, statin therapy should be discontinued. Diabetes mellitus: Patients at risk (fasting glucose 5.6 to 6.9 mmol/L, BMI>30kg/m², raised triglycerides, hypertension) should be monitored both clinically and biochemically according to national guidelines. Excipients: ATOZET contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take this medicine. ADVERSE EVENTS: Common adverse reactions (≥1/100 <1/10): Include diarrhoea and myalgia. In controlled clinical trials, the incidence of clinically important elevations in serum transaminases (ALT and/or AST ≥3 X ULN, consecutive) was 0.6% for patients treated with ATOZET. These elevations were generally asymptomatic, not associated with cholestasis, and returned to baseline spontaneously or after discontinuation of therapy.Please consult the full prescribing information for detailed adverse events.
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Dear Reader,

Welcome to the first issue of 2026. As we step into a new year, we also step into new frontiers of medical science and patient care.

In our Feature Story, we explore how lipid management for cardiovascular disease (CVD) prevention is entering a transformative phase. Two converging trends are reshaping the field: earlier intervention—guided by the principle "the earlier, the better"—and broader strategies that address residual risk beyond low-density lipoprotein cholesterol (LDL-C). Together, these approaches signal a more proactive and comprehensive era in cardiovascular health.

Our Focus Section turns to World Cancer Day, observed annually on 4 February. The 2025–2027 theme, "United by Unique," calls for a fundamental shift in how cancer care is understood and delivered. It challenges us to move from systems built around diseases to systems designed around people—recognizing individuality as the cornerstone of progress in oncology.

In Industry Update, we spotlight key developments across multiple therapeutic areas:

- Dyslipidemia Management – Insights from the 2025 update of the 2019 ESC/EAS Guidelines, optimizing the therapeutic landscape.
- Migraine Care – How CGRP treatments have exceeded trial expectations, offering optimism for the future while underscoring the importance of tolerability for patients.
- Hematology Spotlight – 1) The emerging role of Zanubrutinib in countering follicular lymphoma; 2) Exploring pathways toward curing Hodgkin's lymphoma and empowering patients to thrive fearlessly in the years ahead.

As always, our mission is to bring you timely, thoughtful, and clinically relevant perspectives that illuminate the evolving landscape of medicine. May this issue inspire reflection, spark dialogue, and strengthen our shared commitment to advancing patient-centered care.

Warm regards,

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

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by Dr. Feng Xue

The Earlier The Better: The New Frontiers of Lipid Research for Cardiovascular Disease Prevention

Lipid management for cardiovascular disease (CVD) prevention is entering a new phase defined by two converging trends: earlier intervention ("the earlier the better") and broader targeting of residual risk beyond low-density lipoprotein cholesterol (LDL-C). Recent trial readouts and guideline updates (2025–2026) have reinforced the principle that sustained, deep lowering of atherogenic lipoproteins—especially LDL-C and apolipoprotein B (apoB)—reduces future events, while also elevating triglyceride-rich lipoproteins, lipoprotein(a) [Lp(a)], and metabolic comorbidities as major contributors to persistent risk.[1,2] The field's most visible breakthroughs include (1) expansion of proprotein convertase subtilisin/kexin type 9 (PCSK9) therapy into event reduction for high-risk patients without prior myocardial infarction (MI)/stroke (primary prevention), (2) the emergence of oral PCSK9 inhibition as a potentially adherence-transforming modality, (3) pivotal evidence that targeting apolipoprotein C-III (apoC-III) can meaningfully reduce severe hypertriglyceridemia and pancreatitis events, and (4) an accelerating race to develop Lp(a)-lowering agents with outcomes data anticipated in 2026.[3,4,5,6] Meanwhile, guidelines in Europe and North America increasingly emphasize risk-based intensification, earlier combination therapy, and "lower for longer" LDL-C strategies.[1] Taken together, these developments suggest a coming era of personalized lipid prevention that is earlier, more aggressive, and mechanistically broader than the statin-only paradigm of prior decades.

Why "The Earlier The Better" Has Become the Organizing Principle

For years, clinicians have known that LDL cholesterol contributes causally to atherosclerosis, but recent discussions in preventive cardiology have sharpened the message: waiting to intensify therapy leaves patients accumulating arterial plaque and "lipid burden" that is harder to reverse later. At the 2025 National Lipid Association (NLA) Scientific Sessions, experts underscored a shift away from a slow, stepwise "treat-to-target" mindset toward rapid initiation and early combination therapy, especially for high-risk patients.[7]

This clinical reframing is echoed in the NLA's 2025 guidance—explicitly summarized as "Lower for Longer is Better"—which emphasizes that maintaining LDL-C at very low levels long-term is both safe and essential for lowering atherosclerotic cardiovascular disease (ASCVD) risk.[8] In parallel, European guidance updates released during ESC Congress 2025 focus on optimizing lipid management across complex populations (e.g., acute coronary syndrome, cancer,

human immunodeficiency virus [HIV]), reinforcing the need to reduce cardiovascular risk with individualized approaches and newer LDL-lowering options for those who cannot tolerate statins.[1]

As a whole, "The earlier the better" is no longer just a slogan; it reflects a prevention strategy built on earlier risk identification, earlier therapy intensification, and longer duration of protection—especially as novel tools broaden what can be treated.

LDL-C Still Leads—But the Toolkit Is Expanding Rapidly

PCSK9 Inhibitors Move Deeper into Primary Prevention

A major headline from American Heart Association (AHA) 2025 came from the VESALIUS-CV trial, which tested evolocumab in high-risk patients with atherosclerosis or diabetes but without prior myocardial infarction or stroke. The trial showed evolocumab reduced the risk of first major cardiovascular events compared with placebo, with a 25% risk reduction reported in a composite of CHD death, MI, or ischemic stroke. A meaningful LDL-C reduction was also observed (median LDL-C 45 mg/dL at 48 weeks in a substudy).[3,9] This matters because it strengthens the logic of earlier aggressive LDL-C lowering with potent non-statin therapies in patients who have not yet had an event but are at high risk.

Oral PCSK9 Inhibition: A Potential Adherence Breakthrough

Injectable PCSK9 therapies are effective yet historically underused in some settings. An important development is the progress of enlicitide decanoate (MK-0616), an investigational oral PCSK9 inhibitor.

Positive topline results have been recently announced from the Phase 3 CORALreef (HeFH and AddOn) studies, noting statistically significant, clinically meaningful LDL-C reductions and no clinically meaningful differences in adverse events versus comparators for adults with hyperlipidemia already on lipid-lowering therapies. This Phase 3 program includes trials in heterozygous familial hypercholesterolemia (HeFH), hypercholesterolemia with add-on comparisons, and a large outcomes study targeting time to first major adverse cardiovascular events.[10]

Importantly, CORALreef HeFH demonstrated an approximately 58% LDL-C reduction at 24 weeks (placebo-adjusted) and sustained efficacy through 52 weeks of treatment, with reductions in non-HDL-C, apoB, and Lp(a) also observed.[11]

If oral PCSK9 therapy proves scalable and durable in real-world practice, it may reduce barriers linked to injections and could materially improve long-

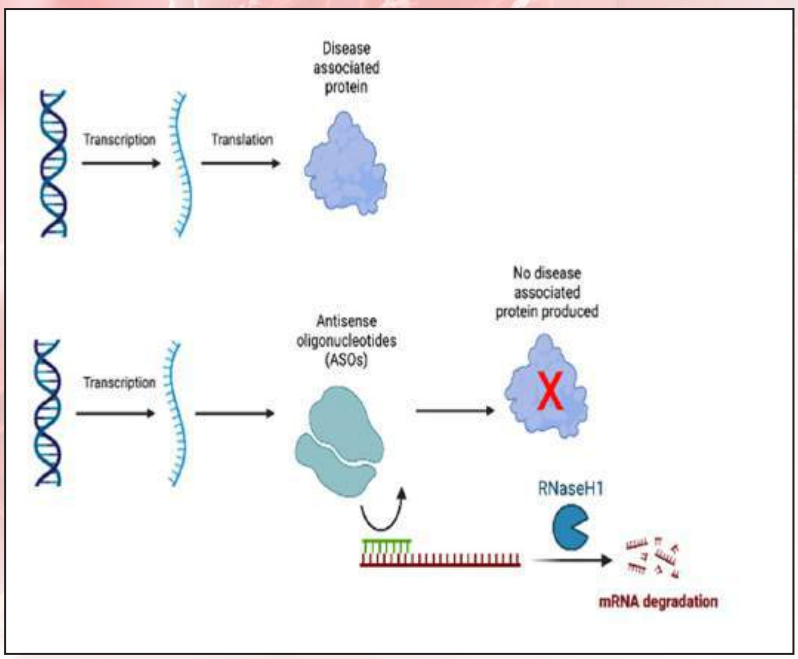

Figure 1. *The mechanism of action of ASOs.[12] ASO, antisense oligonucleotides; mRNA, messenger ribonucleic acid; RNaseH1, Ribonuclease H1.*

term adherence—a critical determinant of prevention benefits.

Triglycerides and Remnant Risk: From "Secondary Marker" to Actionable Target

ApoC-III Inhibition: Pivotal Evidence in Severe Hypertriglyceridemia

While LDL-C remains central, triglyceride-rich lipoproteins and remnants increasingly represent "residual risk." This is especially dramatic in severe hypertriglyceridemia, where pancreatitis risk is high and standard care is often insufficient. In recent years there is a growing trend of using antisense oligonucleotides (ASO) to treat lipid disorders. ASOs are short, synthetic, single-stranded nucleic acids that bind to specific mRNA, preventing the translation of proteins involved in lipid metabolism (**Figure 1**).[12]

Two pivotal Phase 3 trials—CORE-TIMI 72a and CORE2-TIMI 72b—tested olezarsen, an ASO targeting apoC-III mRNA. The NEJM publication reports large placebo-adjusted triglyceride reductions at 6 months, with significant improvements in apoC-III and remnant measures; and importantly, a lower incidence of acute pancreatitis across both trials (mean rate ratio 0.15). The trial summary of the American College of Cardiology (ACC) similarly highlights significant triglyceride reductions and decreased pancreatitis incidence, with detailed baseline and follow-up triglyceride values and a favorable overall adverse-event profile, though with some safety signals (e.g., liver enzyme elevations, thrombocytopenia more frequent at higher dose) consistent with close monitoring.[13]

These outcomes have been generally considered as a potential paradigm change for severe hypertriglyceridemia, emphasizing the scale of triglyceride lowering and pancreatitis event reduction on top of standard-of-care therapy. From the prevention perspective, even though these trials focus on a very high-risk lipid phenotype, they validate apoC-III as a mechanistic target and push triglyceride-rich particle biology toward the center of CVD prevention discussions.

Triple-Agonist Metabolic Approaches: DR10624 as a New Concept

Another late-breaking 2025 development is DR10624, described as a first-in-class medication activating FGF21, glucagon, and GLP-1 receptors. The AHA reported that, in a small Phase 2 trial, DR10624 lowered triglycerides in most patients by more than 60% and reduced liver fat by about 63%, an important finding given the overlap between severe hypertriglyceridemia and fatty liver disease. The ACC also provided additional details on dosing arms and response rates, noting that nearly 90% of treated patients achieved triglycerides below 500

mg/dL in this short, 12-week trial. The corresponding ClinicalTrials.gov record confirms the Phase 2 design and completion timeline.[14,15]

These data are preliminary (conference-level evidence), but they illustrate a broader trend: lipid prevention is increasingly intertwined with metabolic therapeutics that influence adiposity, hepatic steatosis, insulin resistance, and lipoprotein flux—not just LDL receptor biology.

Lp(a): The Most Anticipated Outcomes Story in Lipid Prevention

Why Lp(a) Is Rising to the Top

Lp(a) is widely recognized as a genetically determined, independent risk factor that is not meaningfully lowered by lifestyle or many standard lipid drugs. A 2026 editorial in the Journal of Clinical Lipidology emphasizes that multiple phase 3 programs are underway using different modalities—ASOs (e.g., pelacarsen), siRNAs (e.g., olpasiran, SLN360/zerlasiran, lepodisiran), and even oral small molecules (e.g., muvalaplin)—with several cardiovascular outcomes trials expected to complete in 2026.[16]

Pelacarsen: Timing and Trial Scale

The pelacarsen outcomes trial Lp(a)HORIZON is registered on ClinicalTrials.gov with an estimated primary completion in early 2026 and enrollment exceeding 8,000 participants. It is expected that the Phase 3 pelacarsen data will be available in the first half of 2026, reflecting event accrual timing in this event-driven trial.[17]

Olpasiran and Other Modalities

While not itself an outcomes readout yet, earlier phase data and continuing development for olpasiran have catalyzed broad interest. Industry reporting notes that olpasiran's mid-stage results showed substantial Lp(a) lowering and that phase 3 programs are designed to test whether this translates into fewer cardiovascular events.[18]

Of note, if ongoing trials show that Lp(a)-lowering reduces hard outcomes, prevention strategies may soon include routine Lp(a) measurement and targeted therapy in genetically predisposed patients—representing a true expansion beyond LDL-centric models.[16]

Residual Risk Is Bigger Than LDL: ApoB, Remnants, and Multi-Target Strategies

A 2025 review in the European Heart Journal summarizes the "evolving landscape" of lipid lowering, framing LDL-C as primary but highlighting triglycerides, apoB, and Lp(a) as key drivers of residual risk. It also outlines established and emerging targets: PCSK9 (including evolocumab, inclisiran, and newer agents), ezetimibe, bempedoic acid, and emerging therapies such as ANGPTL3 and apoC-III inhibitors, and revisited CETP inhibition.[19]

This framework helps connect the latest trial headlines: PCSK9 inhibition with stronger evidence across prevention stages (secondary and high-risk primary prevention), ApoC-III inhibition (olezarsen) showing that triglyceride-rich particles and pancreatitis risk can be modified with modern nucleic acid therapeutics, Lp(a) poised to be the next major frontier if outcomes trials confirm benefit, and oral modalities [oral PCSK9, oral Lp(a) approaches] could broaden reach and adherence.

Prevention Beyond Pills: Lifestyle, Food Systems, and Implementation Science

Although therapeutics dominate headlines, recent prevention trial summaries from AHA 2025 remind us that lipid risk is deeply shaped by social and behavioral context. A 2026 review of AHA 2025 prevention trials notes that home-delivered DASH-style groceries combined with brief counseling improved systolic blood pressure and LDL-C in food-insecure urban settings (GoFresh), and that other programs achieved durable improvements in cardiometabolic risk factors.[20]

For lipid prevention in the real world, implementation details—access, affordability, medication persistence, and supportive environments—often determine whether "trial efficacy" becomes "population impact." Oral PCSK9 inhibitors and simplified LDL management guidance may be powerful partly because they can reduce friction in long-term treatment pathways.[21]

Practical Implications: What the "Latest" Means for Clinicians and Health Systems

A New Default: Earlier Risk Stratification and Faster Intensification

With guidelines emphasizing long-term low LDL ("lower for longer"), clinicians may increasingly: identify high-risk individuals earlier using modern risk algorithms and risk enhancers; intensify lipid therapy earlier via combination regimens; and consider potent non-statins sooner in appropriate high-risk groups.

A Broader Biomarker Set: ApoB and Lp(a) as Routine?

The attention to apoB, triglyceride-rich remnants, and Lp(a) suggests lipid clinics will increasingly track beyond LDL-C alone. The Journal of Clinical Lipidology editorial notes that many guidelines recommend measuring Lp(a) at least once in a lifetime, and anticipates multiple

Lp(a) outcomes trials completing in 2026, which could change practice patterns.[16]

Conclusion

Lipid research in 2025–2026 is redefining CVD prevention around a central message: the earlier the better—earlier identification of risk, earlier intensification of therapy, and longer duration of exposure to protective lipid levels. This shift is reinforced by major guideline and consensus updates emphasizing "lower for longer" LDL-C strategies and simplified treatment pathways.

At the same time, the science has moved decisively beyond LDL-C alone. Pivotal evidence for apoC-III inhibition demonstrates that severe triglyceride-rich lipoprotein disorders can be treated in ways that reduce clinically meaningful events like pancreatitis—validating remnant biology as an actionable pathway and strengthening the case for targeting residual risk. The emergence of oral PCSK9 inhibition points to a future where powerful LDL lowering could become more accessible and adherable for broader populations. Meanwhile, Lp(a) stands as the most anticipated frontier, with multiple outcomes trials expected to read out in 2026—potentially ushering in a new era of genetically targeted prevention.

Taken together, these developments suggest the next decade of lipid prevention will be defined by earlier and more personalized intervention, guided by a wider set of lipoprotein targets and delivered through more varied modalities—from injectables to daily pills and RNA therapeutics—while continuing to rely on scalable lifestyle and community interventions to make prevention real at the population level.

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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.

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by Dr. Roy Lau

Optimizing the Therapeutic Landscape in Managing Dyslipidemia – A Discussion on the 2025 Update of the 2019 ESC/EAS Guidelines

Prof. Lau Chu Pak
Specialist in Cardiology
Honorary Clinical Professor
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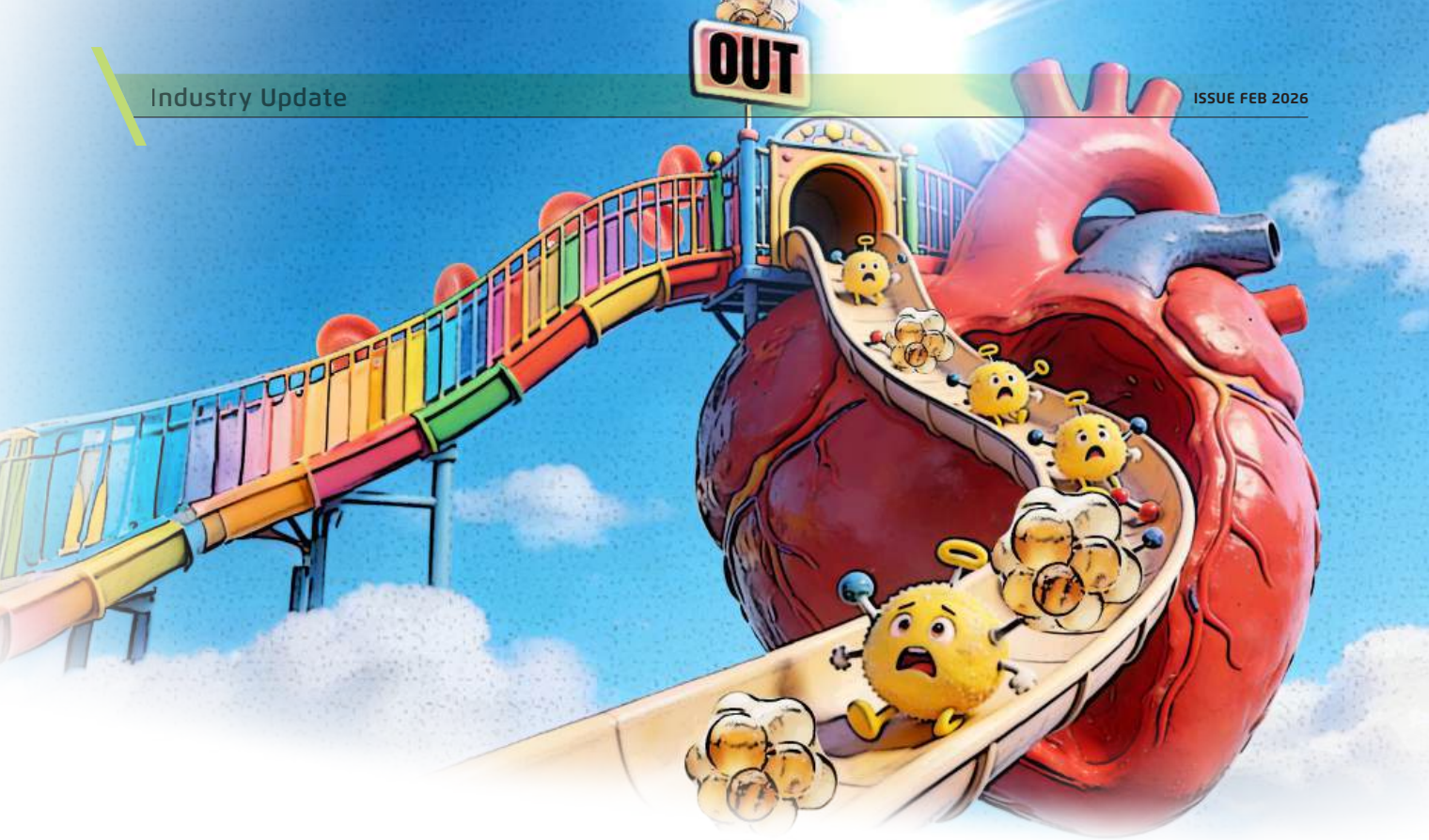
Since the publication of the 2019 European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) Guidelines for the management of dyslipidemia, various landmark clinical trials regarding therapies for dyslipidemia have been published. Accordingly, the ESC Clinical Practice Guidelines Committee has recently announced the 2025 Focused Update, which addresses the changes in recommendations for the treatment of dyslipidemia based on the newly reported evidence[1]. To highlight the clinical implications of the updated guidelines, Prof. Lau Chu Pak was invited to share his insights into the key updates. Particularly, Prof. Lau also discussed the roles of statin-based combined therapies in optimizing dyslipidemia management.

A Glance at the 2025 Focused Update

The 2025 Focused Update has incorporated the findings of several randomized controlled trials (RCTs) that might change patient management ahead of the next scheduled full dyslipidemia guidelines. Prof. Lau outlined that the explicit classification of the "Extreme risk" category on top of the existing "Very high risk" is a key focus of the updated guidelines. Patients with atherosclerotic cardiovascular disease (ASCVD) who experience recurrent vascular events while taking maximally tolerated statin-based therapy, or those who have polyvascular arterial disease are classified as having an extreme risk of cardiovascular (CV) events[1].

Prof. Lau addressed that the updated risk classification precisely indicates the recommended treatment target for low-density lipoprotein cholesterol (LDL-C) for each risk category (**Figure 1**)[1], hence guiding the appropriate treatments. "Patients with documented ASCVD, such as with significant plaque on coronary computed tomography (CT) scan, are classified as "Very high risk" under the updated guidelines, and the recommended treatment target for LDL-C is <1.4 mmol/L and ≥50% reduction from baseline," he noted. Remarkably, the treatment target for LDL-C is <1.0 mmol/L and ≥50% reduction from baseline for the Extreme risk category[1].

By virtue of the aggressive LDL-C goal for patients at extreme risk, Prof. Lau stated that most of these patients are already on statin therapy and thus will require add-on medications to achieve the treatment target. Of note, the reduction in the risk of CV events with ezetimibe in the absence of statin therapy in patients aged ≥75 years and without history of coronary artery disease was demonstrated in the EWTOPIA 75 trial[2]. In this regard, the use of non-statin therapies has been highlighted in the updated guidelines. For instance, the addition of bempedoic acid (BA) to the maximally tolerated dose of statin, with or without ezetimibe, is recommended in patients at high or very



high risk to achieve the LDL-C goal. Prof. Lau quoted that the oral combined treatments would reduce LDL-C by 58-68% (**Figure 2**)[1].

The Role of Statin-based Combined Therapies in Managing Dyslipidemia

Achieving the recommended LDL-C goals can be clinically challenging. Notably, the reported mean LDL-C reduction with monotherapy of a moderate-intensity statin was 30%, whereas those with ezetimibe and BA monotherapy were only 20% and 23%, respectively[1].

In response to the inquiry on first-line therapy for LDL-C lowering, Prof. Lau emphasized that the foremost consideration is whether primary or secondary prevention is required. "A more aggressive treatment approach is needed for secondary prevention to substantially and rapidly reduce the LDL-C level,

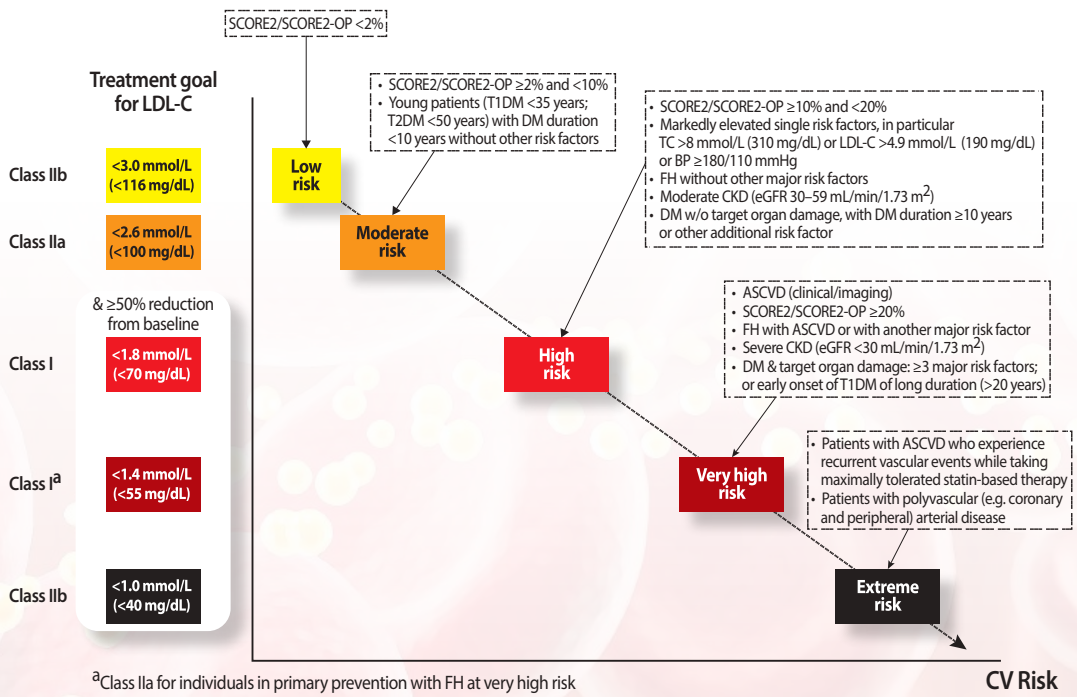


Figure 1: Treatment goals for LDL-C across categories of total CV risk[1], BP: blood pressure; CKD: chronic kidney disease; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; FH: familial hypercholesterolemia; SCORE2: Systematic Coronary Risk Evaluation 2; SCORE2-OP: Systematic Coronary Risk Evaluation 2-Older Persons; TC: total cholesterol level

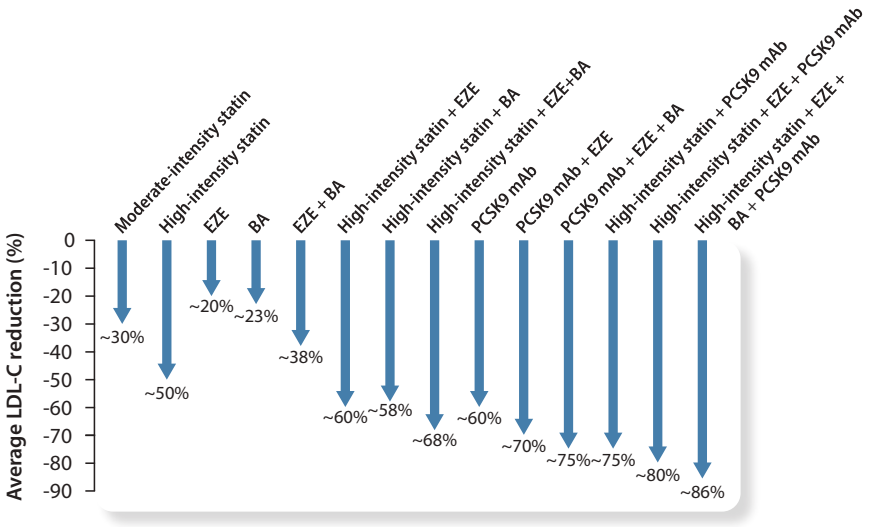


Figure 2: *Average reduction in low-density lipoprotein cholesterol levels with different pharmacological therapies[1], BA: bempedoic acid, EZE: ezetimibe, PCSK9 mAb: proprotein convertase subtilisin-kexin type 9 monoclonal antibodies*

especially in patients with a high baseline LDL-C level," he opined. In contrast, a more gradual up-titration in primary prevention.

A former study by Kytö *et al*. (2022) indicated that patients not using statins early after myocardial infarction (MI) had higher risks of all-cause mortality and major adverse cardiovascular event[3]. Besides, it has been reported that post-percutaneous coronary intervention (PCI) statin treatment significantly reduced the incidence of cardiac death and recurrent MI compared to those without statins[4]. Thus, Prof. Lau stressed that combined treatment with the highest tolerable statin and add-on therapy should be initiated as early as possible for patients with MI or those who have undergone PCI.

Apart from MI and PCI, Prof. Lau stressed that the baseline LDL-C of patients has to be considered. If a 40-50% LDL-C reduction is required, combined treatment of moderate-intensity statin and add-on therapy is recommended rather than high-intensity statin due to better tolerability. Indeed, combined moderate-intensity statin and ezetimibe has been reported to provide noninferior efficacy to high-intensity statins for LDL-C reduction and CVD prevention, with a lower risk of side effects and better treatment adherence[5].

Furthermore, Prof. Lau highlighted the importance of considering side effect profiles and patient adherence when selecting LDL-C lowering therapies. Of note, different intensities and types of statin therapy may have different muscle side effects, and other side effects like liver dysfunction and gout have to be considered. Most of these side effects are readily reversible[6]. Practically, injectable medications may be avoided in some patients with needle phobia to achieve the target LDL-C level.

A Closer Look at the Efficacy of Combined Therapy in Controlling LDL-C Level

As statin-based treatments are the mainstay of LDL-C control, the comparative efficacy of statin monotherapy and statin-based combined therapies has attracted the interest of researchers and clinicians. Recently, a clinical study using medication prescription data and including 31,993 patients after PCI from a national cohort by Lee *et al*. (2024) demonstrated that combined therapy of moderate-intensity atorvastatin and ezetimibe was associated with a significantly lower incidence of 3-year composite of CV events (HR: 0.81, p<0.001, **Figure 3**), statin discontinuation (HR: 0.81, p<0.001), and new-onset diabetes requiring medication (HR: 0.80, p=0.002) than high-intensity atorvastatin monotherapy[7]. The findings suggested that the combined therapy would result in more favorable outcomes and better drug compliance than high-intensity statin.

Prof. Lau commented that the results support the combined therapy as a first-line option. He further noted that the dosage of statin can be increased as appropriate. As the combined therapy of moderate-intensity atorvastatin and ezetimibe is now available as a single-pill regimen, the treatment is expected to improve patient adherence, particularly when polypharmacy is a concern.

Strategies for Managing LDL-C in Patients with Statin Intolerance

Despite the established clinical benefits, the use of statins can be undermined in practice due to true or perceived intolerance. In this regard, the National Lipid Association (NLA) updated its working definition of

statin intolerance in 2022, categorizing it as either complete or partial. Moreover, the NLA statement reasserts that a minimum of two statins should be trialed, at least one at the lowest approved daily dosage, to determine statin intolerance[8].

Prof. Lau described that complete statin intolerance refers to cases in which statins are not tolerable at any lipid-lowering dose, whereas partial intolerance refers to the improved tolerance after a reduction in the maximally tolerated statin dose. While complete statin intolerance is practically rare, most patients can tolerate statins at certain dosages, and the side effects are dose dependent, which occurs more with high-intensity statins[9].

For suspicious cases of statin intolerance, Prof. Lau advised ruling out any secondary causes of the reported symptoms first. "Some patients may have hypothyroidism or orthopedic problems, which lead to the symptoms. Some drug interactions may trigger the symptoms as well," he noted. Then, a 2-week statin suspension can be trialed. If side effects persist, statin treatment can be resumed as the symptoms are unlikely to be statin related. Besides, if side effects are relieved with a reduced statin dosage, add-on therapy can be prescribed to maintain LDL-C lowering efficacy.

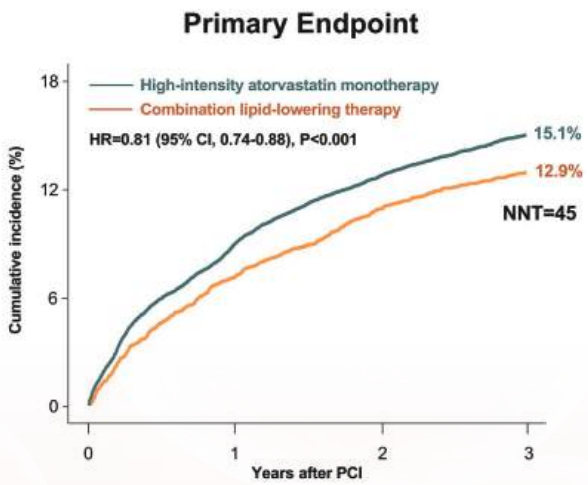


Figure 3: *Time-to-event curves for composite of CV events[7], NNT: number needed to treat*

Early Lowering LDL-C Optimizes Cardiovascular Risk Reduction

The 2025 Focused Update of ESC Guidelines redefines the CV risk categories and guides the treatment to achieve the specific LDL-C goals. Prof. Lau emphasized that LDL-C is a key modifiable risk factor for CV events. Thus, the lower LDL-C levels, the better. Particularly, early achievement of the LDL-C goal is needed for secondary prevention in high-risk patients. "Doublet or even triplet combined treatment may be needed for rapid LDL-C lowering in patients with extreme risk," Prof. Lau commented.

As a final remark, Prof. Lau reminded that a high lipoprotein(a) [Lp(a)] level is an important risk modifier indicating increased CV risk, and a more aggressive treatment approach should be considered[1]. Practically, substantial LDL-C reduction is needed in most patients, and combined therapies are advisable. Regarding intolerance to high-intensity statins, moderate-intensity statins with add-on therapy can be considered. Last but not the least, Prof. Lau emphasized that lifestyle interventions are essential for all patients. "Red meats and fatty foods should be avoided, yet plenty of green vegetables and exercise are highly desirable," he advised.

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Enter an Era of Optimism and Clinical Impact with CGRP Migraine Therapy

by Jasmine Lai

Professor Piero Barbanti, MD, PhD

Professor of Neurology, San Raffaele University, Rome
Director of the Headache and Pain Unit, IRCCS San Raffaele, Rome
Member of the Board of Trustees of the International Headache Society

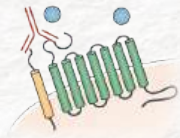
CGRP inhibitors have redefined migraine prevention, leaving the troubles of non-specific, conventional oral therapies behind. The spotlight is now on their real-world, long-term benefit—particularly as migraine often occurs in complex, comorbid patients. At the 9th Hong Kong Neurological Congress cum 38th Annual Scientific Meeting of The Hong Kong Neurological Society, Professor Piero Barbanti shared how CGRP treatments have delivered beyond trial expectations, and expressed his optimism in the path forward for migraine management—reminding us that above all, tolerability remains key for patients.

Effectiveness At What Cost? The Optimal Efficacy-Tolerability Ratio that Patients Want

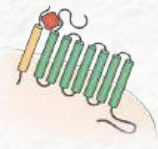
CGRP receptor blockade affects amylin receptor GI functions[1]:

- Reduced food intake
- Gastric stasis
- Glucose homeostasis

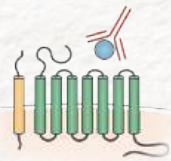
CGRP-receptor blockers[2]:



mAb
e.g. erenumab

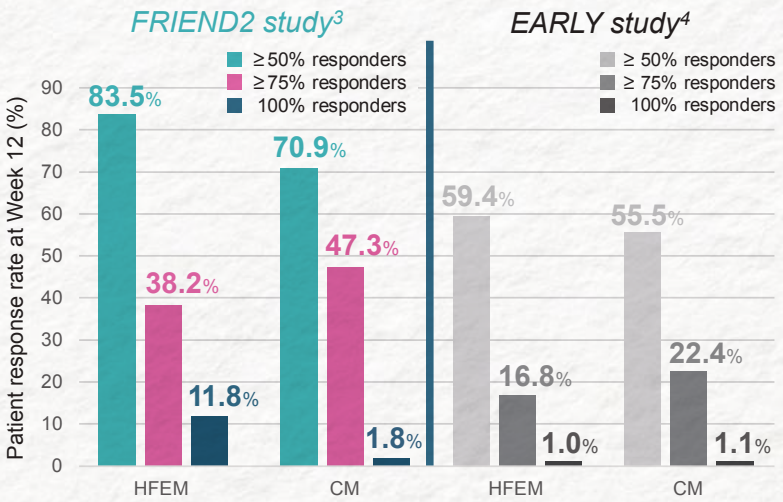


antagonist
e.g. atogepant



Fremanezumab is an Anti-CGRP mAb Without Receptor Blockade and Significant GI Effects[3]

RWE Affirms Fremanezumab's Greater Effectiveness and Tolerability



FRIEND2: A prospective, cohort, real-life study at 28 headache centres on 410 adult patients (146 for efficacy analysis) affected by HFEM or CM with multiple preventive treatment failures, who were prescribed subcutaneous fremanezumab 225 mg monthly/675 mg quarterly) for ≥24 weeks[3].

EARLY: A multicentre, prospective, cohort, real-life study at nine Italian headache centres with 372 adult patients affected by HFEM or CM, who were treated with subcutaneous erenumab 70 mg every 4 weeks for 6 to 12 months[4].

Fremanezumab is Effective in Migraine Patients with Major Depressive Disorder[5]

UNITE RCT[5]:

≥50% reduction in monthly migraine days (MMD):

- ***As Early As Week 4***
  P<0.001 vs placebo
- ***Maintained to Week 12***
  P=0.002 vs placebo

Depression score at Week 8:

HAM-D 17 score reduction -6.0 = **Clinically meaningful improvement met**

from a baseline of moderate-to-severe depression

irrespective of MMD reduction

UNITE: 28 week, multicentre, randomised clinical trial on 353 adult patients with migraine and comorbid major depressive disorder confirmed by a psychiatrist. Patients were randomised to receive fremanezumab (225 mg monthly) or placebo[5].

CGRP Treatment has an Exciting Future Ahead...

Evidence for long-term treatment ≥3 months[6,7]

≥50%, ≥75% and 100% new responders even up to 48 weeks

Only **8.7%** ***≥50% non-response within 48 weeks***

Potential long-term disease modifying effects[8]

Fewer migraine relapses even when treatment is discontinued over 3 years

P<0.001 for 1st vs 3rd time treatment was discontinued

Fremanezumab is the CGRP That Keeps Your Patients In Mind

The Only CGRP with Flexible Monthly/ Quarterly Dosing[9]

Allows patients to forget about their condition unlike oral pills

Effective Across Migraine Subtypes (EM, CM, MOH)[9]

Plus future studies with common comorbidities (fibromyalgia, sleep disorders)

Injection and Without Loading Dose[9]

Better adherence, faster effects

Abbreviations: AE, adverse events; CGRP, calcitonin gene-related peptide; CM, chronic migraine; EM, episodic migraine; GI, gastrointestinal; HAM-D 17, Hamilton Depression Rating Scale–17 Items; HFEM, high-frequency episodic migraine; mAb, monoclonal antibody; MMD, monthly migraine days; MOH, medication-overuse headache

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by Dr. Roy Lau

Uncovering the Role of Zanubrutinib in Countering Follicular Lymphoma

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Follicular lymphoma (FL) is an indolent form of non-Hodgkin's lymphoma (NHL) that originates from germinal centre B cells[1] and is the second most common NHL subtype worldwide. Although first-line treatment achieves a complete response (CR) and sustained remission in most patients with FL, a substantial proportion of the patients experience serial relapses, become refractory to treatment, or develop histologic transformation to aggressive B-cell lymphoma[2]. Therefore, new therapies with promising efficacy and safety profile are highly desirable. While Obinutuzumab-based treatment has been reported to yield survival benefits in patients with FL[3], recent trials have demonstrated that the combined treatment of Zanubrutinib and Obinutuzumab results in further improved progression-free survival (PFS), with a preferable tolerability[2]. In a recent sharing, Dr. Chandramouli Nagarajan presented the clinical findings of Zanubrutinib-based treatment and discussed its potential role in managing FL.

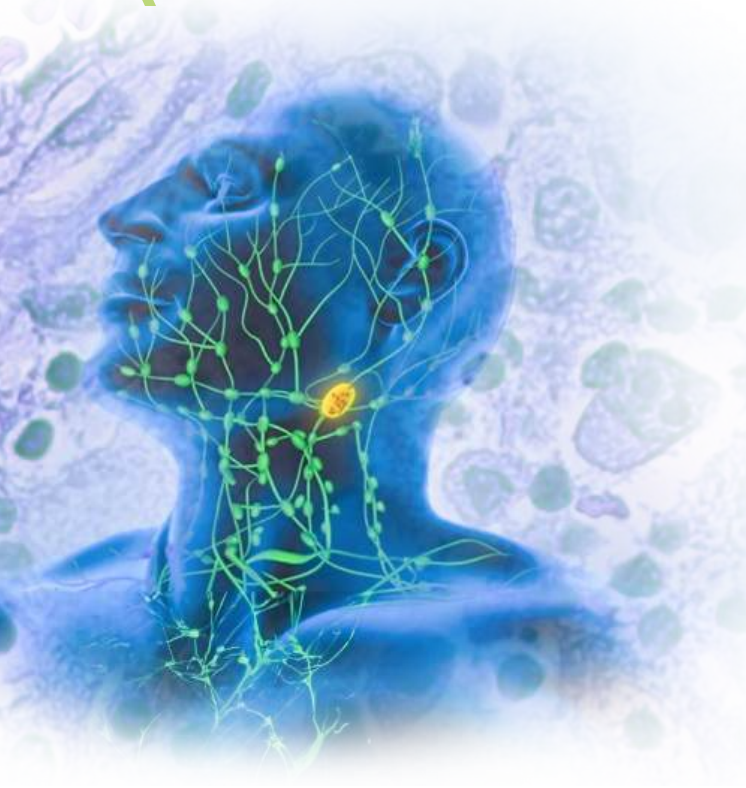
Translating Research Findings into Clinical Benefits

FL is one of the most common indolent NHL subtypes in Western countries. For instance, Gupta *et al*. (2022) reported that the incidence of FL reached 3.18 cases per 100,000 people annually in the United States, accounting for approximately 20-25% of all NHLs[1]. Dr. Nagarajan highlighted that FL is more prevalent among older adults, with the median age of FL patients being 65 years old. Moreover, FL appears to occur more frequently in male patients, with a male-to-female ratio of 1.2:1[1]. Notably, differences in incidence rates for FL by ethnicity were observed, with the highest rates in Caucasians, which suggests potential genetic differences in susceptibility to the disease[4].

Key Principles in Follicular Lymphoma

FL is a biologically heterogeneous disease with a diverse range of clinical presentations. However, most patients present with an indolent disease course, with continuous patterns of relapse and progressively shorter disease-control intervals with each line of treatment[5]. Although FL is still considered incurable, the life expectancy for most patients is long, with a 5-year relative survival rate of 90%[6].

The t(14;18) translocation is the genetic hallmark of FL, which gives rise to a BCL2-IGH fusion and is observed in >85% of FL. While the low levels of t(14;18) translocation can be detected in 50-70% of presumably normal adults, higher levels of circulating t(14;18) cells, greater than 1 in 10,000 blood cells, are associated with a 23-fold higher risk of developing FL[4]. Remarkably,



components of the B-cell receptor signalling pathway, such as phosphoinositide 3-kinase (PI3K), Bruton tyrosine kinase (BTK), and spleen tyrosine kinase, are frequently activated in FL[5], suggesting the potential application of kinase inhibitors for treating FL.

"Treatment of FL is primarily based on symptoms rather than stage or biology", Dr. Nagarajan addressed. Indeed, existing literature advocates that FL treatment aims to decrease symptom burden and morbidity, improve quality of life, and prolong survival[1]. Regarding relapsed or refractory (R/R) FL, there is currently no standard management for the condition. Nonetheless, many drug combinations, novel agents, and transplant options have been studied and have demonstrated efficacy.

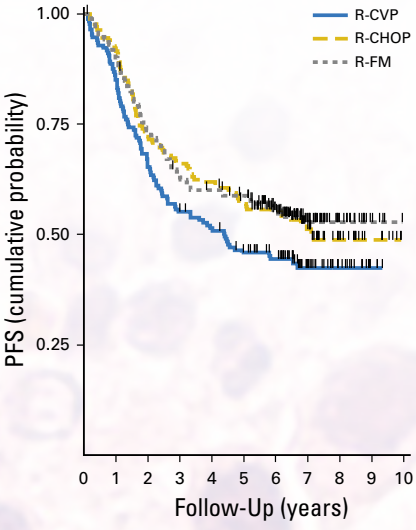


Figure 1: PFS achieved in the FOLL05 trial[7]

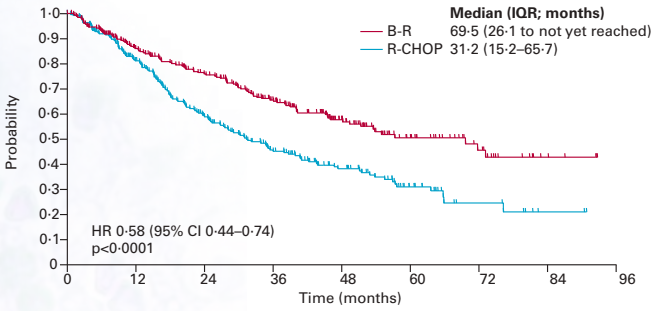


Figure 2. PFS achieved by B-R and R-CHOP[8]

Chemoimmunotherapy for Advanced and Treatment-Naïve Follicular Lymphoma

Practically, the efficacy of anti-CD20 monoclonal antibody has been established. However, the choice of chemotherapy backbone is still controversial. Accordingly, the FOLL05 trial by Luminari *et al*. compared the clinical outcomes achieved by various chemoimmunotherapy (CIT) regimens, including R-CVP (rituximab plus cyclophosphamide, vincristine, and prednisone), R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone), and R-FM (rituximab plus fludarabine and mitoxantrone), in treatment-naïve patients with advanced FL[7].

Based on a median of 7 years follow-up of the FOLL05 trial, the hazard ratio (HR) for PFS adjusted by FL International Prognostic Index 2 versus R-CVP was 0.73 for R-CHOP (p=0.037) and 0.67 for R-FM (p=0.009, **Figure 1**). The 8-year overall survival (OS) rate was 83%, with no significant differences among the study arms[7]. The results thus confirmed the favourable OS with the CIT regimens, but R-CVP was not as effective as R-CHOP and R-FM in enhancing PFS.

In the StiL trial by Rummel *et al*. (2013), the efficacy of bendamustine plus rituximab (B-R) as first-line treatment for patients with indolent and mantle-cell lymphomas was compared with that of R-CHOP. At a median follow-up of 45 months, the median PFS was significantly longer in the B-R group than in the R-CHOP group (69.5 months vs 31.2 months, HR: 0.58, p<0.0001, **Figure 2**). The results also indicated that B-R was better tolerated than R-CHOP[8]. Hence, B-R would be a preferred first-line treatment approach relative to R-CHOP.

Subsequently, the clinical performance of B-R, R-CHOP, or R-CVP in treatment-naïve patients with indolent NHL or mantle-cell lymphoma was evaluated in the BRIGHT trial. The 5-year follow-up results revealed that the PFS rates at 5 years were 65.5% in the B-R group, which was

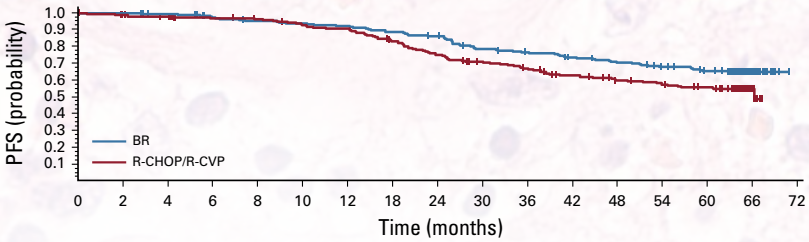


Figure 3. PFS achieved by B-R and R-CHOP/R-CVP[9]

significantly higher than those in the R-CHOP/R-CVP group (55.8%, HR: 0.61, p=0.0025, **Figure 3**). The HR for event-free survival (p=0.002) and duration of response (p=0.0134) also favoured the B-R regimen over R-CHOP/R-CVP. Nonetheless, no significant difference in OS was observed[9]. The results further supported that B-R provided better long-term disease control than R-CHOP/R-CVP.

The Unmet Needs in Managing Follicular Lymphoma

According to the ESMO clinical guidelines, patients with FL are classified as either high-tumour burden, who are usually treated with CIT with or without maintenance, or low-tumour burden, for whom a watch and wait (WW) strategy is recommended until disease progression[10]. Nonetheless, Dr. Nagarajan highlighted the unmet need in FL that about 20% of patients with FL experience disease progression within 2 years of first-line treatment, known as POD24, and consequently have an unfavourable prognosis. It has been reported that the 5-year OS of FL patients experiencing POD24 was 50%, whereas that of the non-POD24 group was 90%[11].

Dr. Nagarajan further addressed that POD24 is a post-treatment endpoint and, therefore, cannot be used to guide upfront treatment decisions. Given that POD24 can be evaluated based on biopsies, it can serve as a tool for identifying high-risk FL patients and should be routinely considered[11].

Zanubrutinib - The Next-generation Bruton Tyrosine Kinase Inhibitor

While biopsy at relapse is essential for ruling out transformation to aggressive histology, prescribing more intensive or novel therapeutic strategies may be beneficial for improving the survival and quality of life (QoL) of patients with R/R FL. In recent years, Bruton tyrosine kinase inhibitors (BTKi) have emerged as promising therapeutic options for R/R FL. Particularly, Zanubrutinib is a potent, specific, and irreversible second-generation covalent BTKi, which achieves deep and durable responses in patients with various B-cell malignancies[12].

The efficacy of Zanubrutinib monotherapy in countering R/R FL was examined in the phase 1/2, open-label, multicentre, single-agent trial by Phillips *et al*. (2022), which involved 20 R/R marginal zone lymphoma (MZL) and 33 R/R FL patients. In patients with R/R FL, the overall response rate (ORR) was 36.4%, and the complete response (CR) rate was 18.2%. After a median follow-up of 33.9 months, the median PFS was 10.4 months. The treatment with Zanubrutinib was generally well tolerated, with most adverse events being grade 2 or lower[12]. The results suggested a favourable benefit-to-risk profile of Zanubrutinib, which could be a promising addition to available therapies for patients with R/R FL.

The Clinical Performance of Zanubrutinib in R/R FL in ROSEWOOD Trial

To illustrate the efficacy of Zanubrutinib in combined therapies against R/R FL, Dr. Nagarajan presented the findings in the ROSEWOOD trial. In the trial, patients with R/R FL who had received at least 2 lines of therapy were randomly assigned at a 2:1 ratio to receive either the combined therapy of Zanubrutinib and Obinutuzumab (ZO), an anti-CD20 therapy, or Obinutuzumab (Ob) monotherapy[2].

After a median follow-up of 20.2 months, the ORR by independent central review (ICR) achieved with ZO treatment (n=145) was 69%, which was significantly higher than that of Ob (n=72, ORR=46%, p=0.001). Of note, the ORR advantage of ZO over Ob did not differ substantially across prespecified subgroups, such as gender, previous lines of therapy, FLIPI risk category, etc. Moreover, the CR rate of the ZO group was 39%, whereas that of Ob was 19% (p=0.004). The partial

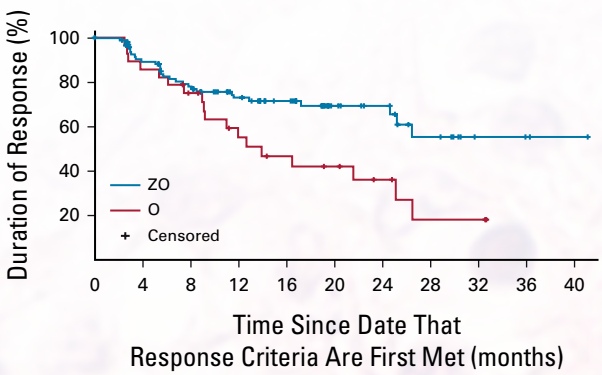


Figure 4. DOR response per ICR by treatment[2]

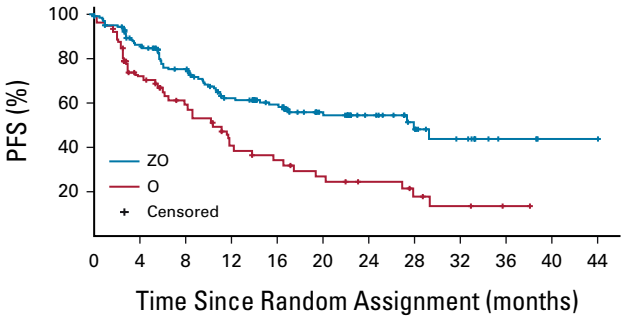


Figure 5. PFS per ICR by treatment[2]

response (PR) rates for the ZO and Ob groups were 30% and 26%, respectively. Importantly, the 18-month duration of response (DOR) rate was 69% in the ZO group and 42% in the Ob group (**Figure 4**)[2].

Regarding survival benefits, the estimated OS rate at 24 months was numerically higher (p=0.085) with ZO (77%) compared to Ob (71%). However, the median PFS of the ZO group (28.0 months) was significantly longer than that of Ob (10.4 months, HR: 0.50, p<0.001, **Figure 5**). In particular, the time to next treatment (TTNT) was not estimable with ZO, which was significantly longer than that achieved with Ob (12.2 months, HR: 0.34, p<0.001, **Figure 6**). Furthermore, the ZO toxicity profile is consistent with the known and tolerable safety profiles of each drug, with no unexpected additional concerns[2]. Based on the results, the ZO treatment demonstrated meaningful efficacy and a manageable safety profile in heavily pretreated patients with R/R FL.

The New Hope for Patients with R/R FL

Recent developments in therapeutics for FL have substantially improved the outcomes for most patients, with survival often lasting a decade or more, and many are functionally cured. Nonetheless, the development of relapsed or refractory disease is still a clinical challenge. As per Dr. Nagarajan, biopsy at relapse is crucial in identifying high-risk FL patients, whereas timely prescription of novel therapeutic strategies lead to better patient outcomes. "An understanding of the patient profiles is important for optimising the individualised therapy," he emphasised.

In view of the results of ROSEWOOD trial, Dr. Nagarajan noted that BTKi is valuable across different low-grade NHLs in combination with anti-CD20 therapies. In addition to BTKis, he looked forward to witnessing the development of newer-generation immunotherapies and the therapeutic benefits they brought to patients with FL.

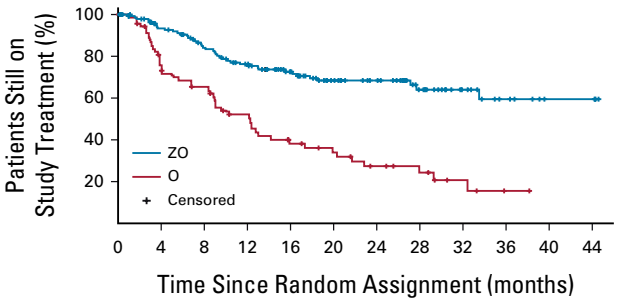


Figure 6. TTNT achieved by ZO and Ob[2]

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by Dr. Mohsin Roshan

Cure Hodgkin's Lymphoma and Thrive Fearlessly in the Future Chapters

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Hodgkin's lymphoma (HL) is a rare monoclonal lymphoid neoplasm that consists of two subtypes: classical HL (cHL- 95% cases) and nodular lymphocyte predominant HL (NLP-HL)[1,2]. Notably, cHL has a bimodal age distribution that initially peaks at age 20-30 years, followed by a subsequent peak between the age 50-70 years[3]. In addition, the incidence of HL in Hong Kong has increased substantially over the last 2-3 years[4]. Remarkably, the treatment paradigm of HL has evolved over the years, making HL a neoplasm with excellent prognosis[5]. To understand the evolution of treatment dogma of HL, we have invited Dr. Tommy Tam to share his insight into the local real-world practice.

Classical HL – A Growing B Cell Malignancy?

HL is a rare monoclonal lymphoid neoplasm characterised by the proliferation of large multinucleated cells, also known as Hodgkin and Reed-sternberg (HRS) cells[2,5]. The incidence of HL in Europe was reported to be around 2-3 per 100,000 individuals[5], while in Hong Kong it fluctuates between 0.6 and 1.2 according to the Hong Kong Cancer Registry, with 81 cases registered in 2021[6]. However, recently published statistics suggested an increase of 6.23% in male cases and a 5.39% increase in cases among females, while the mortality rate in both genders decreased since 2022[4]. Despite these reported findings, Dr. Tam suggested that he did not notice an uptrend in the incidence of HL in his clinical practice. Nevertheless, he explained that the rising incidence may partially be driven by the growing numbers of high-risk individuals (smokers, obesity, hypertension and Epstein-Barr virus [EBV] infection). Moreover, with an increased sensitivity in medical imaging, cases are diagnosed more accurately, thereby contributing to the uptrend of HL incidence.

Diagnostic Difficulties in Diagnosing HL

Patients with cHL, especially in young population, commonly present with persistent, painless superdiaphragmatic lymphadenopathy in neck or supraclavicular fossa. Lymphadenopathy may develop within the mediastinum, which triggers symptoms such as cough, substernal chest pain, or anterior chest wall swelling[7]. Aside from these localised symptoms, HL systemic manifestations include night sweat, unexplained weight loss and recurring fever[7], which are similar in both younger and older populations. Because of these noticeable symptoms, patients usually seek medical consultation promptly, thus making timely diagnosis possible. However, in cases where swollen lymph node is the only noticeable abnormality, a rare misjudgement may occur, Dr. Tam added.

Breaking the Chain of Toxicity

Treatment consideration plays an important role in improving treatment tolerability, optimising treatment outcomes, and facilitating the return to a normal life[8]. The prime concern is the patient's background, particularly the comorbidities such as the cardiovascular function, history of chronic disease and frailty, according to Dr. Tam. Moreover, it is of paramount importance to choose a treatment algorithm with promising efficacy and safety profile, since treatment tolerability and quality of life play a vital role in patients' recovery. In addition, consolidation radiotherapy should be used with caution due to an increased risk of breast cancer in female patients who have previously undergone radiotherapy for HL[9].

With the emergence of various classes of treatment, the breadth of the landscape in advanced cHL treatment has offered physicians and patients options to minimise adverse effects and optimise treatment efficacy[8]. Currently, doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) has replaced escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (eBEACOPP) to become the most widely adopted treatment regimen in HL[10]; however, the long-term toxicity observed in HL survivors remains a pressing issue, and some commonly reported adverse effects include pulmonary toxicity, cardiac dysfunction, and secondary malignancies[11]. Therefore, there is room for improvement by minimising treatment toxicities in the conventional treatment algorithm. Dr. Tam explained that after patients have undergone a few cycles of ABVD, they can be assessed by the positron emission tomography (PET). If response is observed, doses can be lowered, or treatment cycles can be reduced. Specifically, given the well-documented toxicity of bleomycin, the risk of toxicity can be mitigated by removing bleomycin from the combination therapy if patients achieve complete metabolic response upon interim PET scan after 2 cycles of ABVD (iPET2 CMR), as per recent study findings[11–13].

Removing the Barrier to Optimal Outcome

Despite these innovations, barriers to improving the treatment outcomes are still to be overcome. Dr. Tam elaborated on the two main barriers to optimising the treatment outcome: financial difficulty and the elimination of chemotherapeutic agents from the treatment protocol. As we are aware that not everyone has a full medical insurance coverage, the affordability issue may hinder their ability to utilise the newer treatment. In addition, some patients are required to fulfil certain eligibility criteria in order to be covered by the government's subsidy, such as the use of medication in a later line setting. In terms of treatment, Dr. Tam emphasised that the journey to move beyond the reliance on chemotherapy as a mainstream treatment still lies ahead, but the medical community is already moving in the right direction.

Shift of Paradigm from Chemotherapy to Novel Agents

As highlighted, the treatment paradigm has been shifted to prioritise safety and tolerability, owing to the toxicity of chemotherapy[11]. Dr. Tam reiterated that for stage III/IV patients, target therapy is often added to replace the chemotherapy. For instance, anti-cluster of differentiation 30 (anti-CD30) antibody-drug conjugates and anti-programmed cell death protein 1 (anti-PD-1) agents are increasingly prescribed, albeit primarily in the 2nd or 3rd line settings[8]. As abundant evidence demonstrating the efficacy of these medications emerges, moving the prescription of these medications to the first line can be anticipated[8,11]. Thus, brentuximab vedotin + AVD (BV+AVD) are gradually replacing bleomycin with brentuximab vedotin (BV) as this may lower the incidence of pulmonary toxicity while improving the efficacy as compared to ABVD regimen[14].

The ECHELON-1 study, an open-label, multicentred, randomised phase 3 trial included 1,334 patients in

which 664 and 670 patients were randomly assigned to BV+AVD and ABVD groups, respectively[14]. The primary endpoint of ECHELON-1 study was modified progression free survival (PFS), defined as time to disease progression, death, or modified progression (with the latter defined as evidence of noncomplete response after completion of frontline therapy according to review by an independent committee, followed by subsequent anticancer therapy) and the key secondary end point was overall survival, defined as the time from randomisation[14]. At a median follow-up of 24.6 months, the 2-year modified PFS in BV+ AVD and ABVD groups were 82.1% (95% confidence interval [CI]: 78.8-85.0) and 77.2% (95% CI: 73.7-80.4), respectively, a difference of 4.9 percentage points (hazard ratio for event of progression, death, or modified progression, 0.77; 95% CI: 0.60-0.98; p=0.04)[14]. Given the prevalence of the adolescents and young adults (AYA) population in advanced cHL and its significant proportion in the ECHELON-1 trial (accounting for 58% of the intend-to-treat [ITT] population), a subgroup analysis of ECHELON-1 was started in the AYA patients aged from 18 to 39 to evaluate the consistency of the safety and efficacy of BV+AVD regimen at 6 years[15]. Among them, 396 patients received the BV+AVD regimen and 375 received ABVD regimen[15] .

Remarkable consistency in the PFS and OS benefits with the ITT population was demonstrated. A staggering 36% risk reduction in disease progression at 6 years was found in the BV+AVD arm compared to those in the ABVD arm, with the 6-year PFS rate of 86.4% with BV+AVD versus 79.4% with ABVD (HR 0.636; 95% CI: 0.445-0.908; P=0.012)(**Figure 1**)[15]. The younger patients aged 18-29 years showed a similar outcome, with 6-year PFS rate of 87.3% with BV+AVD and 80.0% with ABVD (HR 0.604; 95% CI: 0.378-0.965; *P*=0.033)[15]. Across ages 18 to 39, numerical PFS benefit with BV+AVD versus ABVD regardless of PET2 status was noted. Furthermore, after 71.7 months of median OS follow-up, a striking reduction in death of 60% was discovered, as the estimated 6-year survival rate was 98.2% for BV+AVD arm and 94.9% for the ABVD arm (HR 0.391; 95% CI: 0.161-0.951; P=0.032)[15], thus underscoring the sustained efficacy of BV+AVD in disease control and preventing progression across subgroups.

Since the long-term sequelae of HL treatment have been a concern in long-term survivorship[11,16], adverse events have been analysed in this study. Notably, no impact on fertility was seen in females on BV+AVD regimen, in that BV+AVD arm has a higher pregnancy rate of 23.4% compared to 16.8% in the ABVD arm. Nor did males suffer from infertility, as 31 and 30 partners of the male HL patients were able to become pregnant in BV+AVD and ABVD groups, respectively. As for secondary malignancies, less than 2% of second cancers were found in each arm, which was even lower than the ITT population in ECHELON-1 trial (3.5% with BV+AVD and 4.9% with ABVD)[15,17], thus establishing the long-term safety of BV+AVD regimen. Finally, a higher risk of developing peripheral neuropathy (PN) was identified, with 64% in the BV+AVD arm and 40% in the ABVD arm reported to have any-grade PN. Fortunately, 78% of patients attained a complete resolution and 11% had an improvement at 6 years (**Figure 2**), which means proactive management makes PN a manageable side effect[15].

Harness the Power of the BV+AVD Regimen

To illustrate the benefits of BV+AVD regimen in young adults, Dr. Tam shared a case involving a young female diagnosed with stage 3 cHL. The patient initially presented with chest pain and dyspnoea. The PET scan revealed a large tumour in the mediastinum and a few lesions in other parts of the body. Considering that the patient chose to continue a career in performing art, Dr. Tam believed choosing an efficacious regimen with minimal pulmonary toxicity would be of utmost importance. Added that the patient was young

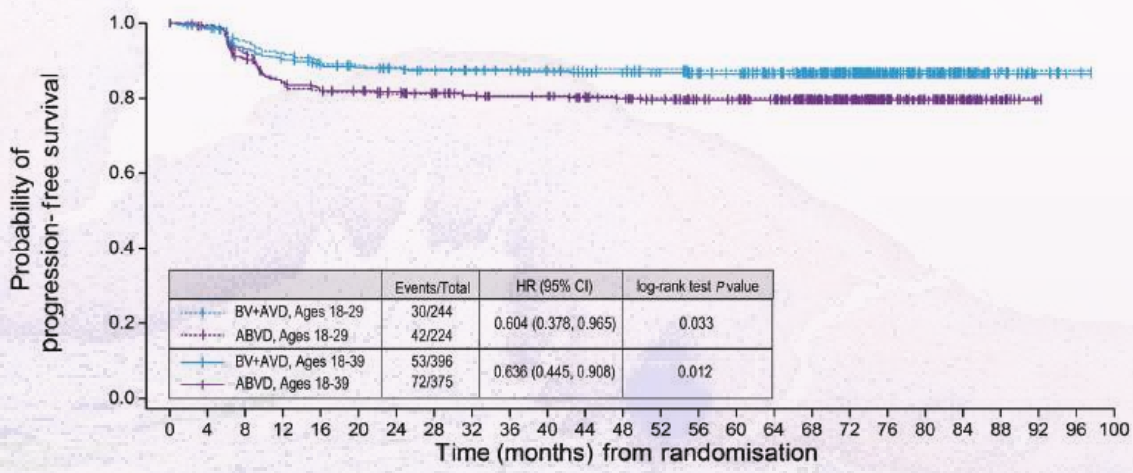

Figure 1. Progression-free survival per investigator since time from randomisation (Adapted from Crosswell H, et al. 2023)[15]

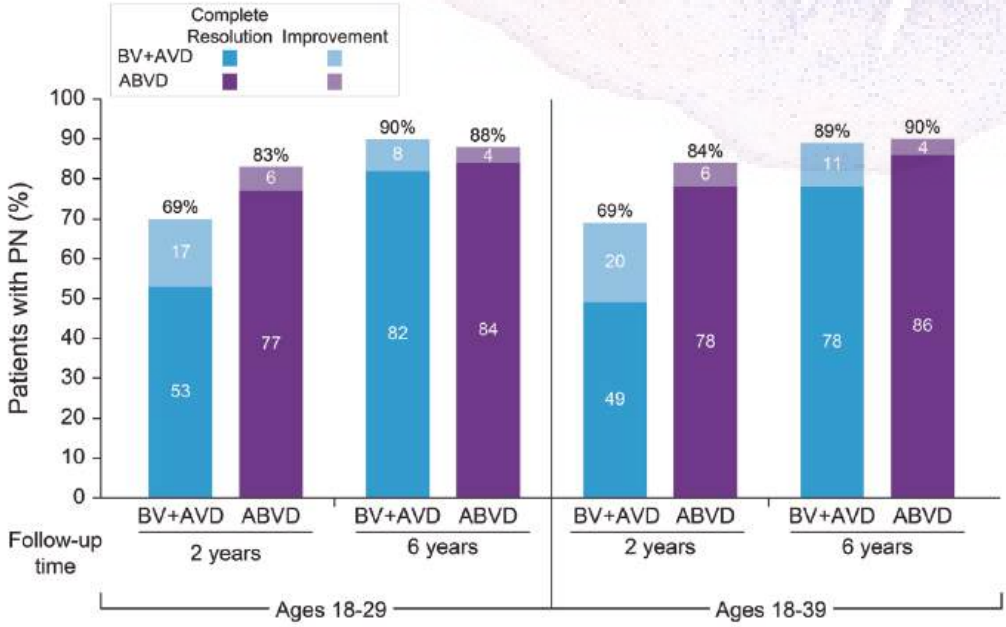

Figure 2. Rate of complete resolution and improvement in peripheral neuropathy analysed at 2 years and 6 years (Adapted from Crosswell H, et al. 2023)[15]

at the time of diagnosis, the risks of secondary diseases resulting from chemotherapeutic agents and radiotherapy were avoided. As a result, Dr. Tam opted for 6 cycles of BV+AVD regimen for the patient, and remarkably, a treatment response was observed only after 1-2 cycles as the chest symptoms resolved. After 6 treatment cycles, the patient achieved complete remission, and had been in remission for 3 years.

Continue Refining the Treatment Protocol

Patients with advanced cHL are often faced with enormous treatment burden and risk of relapse. Thankfully, an effort to minimise the treatment toxicity burden is witnessed with groundbreaking agents and modified treatment algorithms. Additionally, the international data and clinical experience have laid a solid foundation for refining the treatment protocol of advanced cHL[8]. BV+AVD has been utilised by local doctors for some years and the medical community has sufficient clinical experience with the variations of this regimen, according to Dr. Tam. Nevertheless, to maximise the therapeutic benefits of advanced HL treatment, doctors could pay closer attention to the signs exhibited by patients and make prompt dosage adjustments if necessary. BV+AVD regimen showed a superior efficacy compared to the ABVD regimen in treating patients with advanced cHL14. As the new era of cHL treatment ushers a brighter treatment prospectus, it is merely a matter of time for advanced cHL to be treated like a chronic disease.

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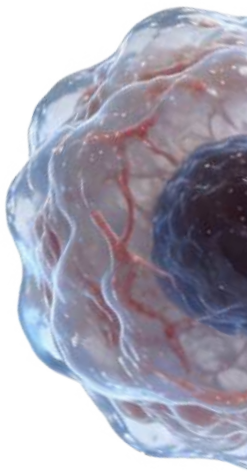
by Dr. Feng Xue



United by Unique: Honoring Every Story on World Cancer Day 2026

World Cancer Day, observed annually on 4 February, is a global moment for reflection, awareness, and action. The 2025–2027 theme, "United by Unique," calls for a fundamental shift in how the world understands and delivers cancer care: from systems built around diseases to systems designed around people. This article explores the meaning behind the theme, why a people-centered model matters, and how individuals, communities, and institutions can work together to build a future in which every person's story guides care. By recognizing that every experience of cancer is unique—and by uniting across sectors and societies—we can create a world that looks beyond the disease and truly sees the person.[1,2,3]

World Cancer Day 2026: More Than a Date on the Calendar

Every year on 4 February, World Cancer Day brings together patients, survivors, caregivers, clinicians, researchers, policymakers, and advocates in a shared purpose: to raise awareness, reduce stigma, promote equitable access to care, and inspire tangible improvements in prevention, diagnosis, treatment, and survivorship. But beyond the statistics and strategies lies a deeper human truth—cancer is never just a medical condition. It touches identity, family, livelihood, hopes, and community.[4]

The theme for 2025–2027, "United by Unique", puts this truth at the center. It reminds us that while cancer is a global challenge, its impact is deeply individual. Two people with the same diagnosis will not have the same journey. Different cultures, ages, languages, genders, incomes, and life circumstances shape how cancer is understood, experienced, and treated. Recognizing and honoring this individuality is not a "nice-to-have"—it is essential to achieving the best outcomes and sustaining dignity at every step of care.[5]

Why "United by Unique" Matters Now

The burden of cancer continues to grow, and so do disparities. People in different regions, income groups, and communities often face unequal access to prevention, early detection, modern therapies, and supportive care. Some face social stigma or legal barriers; others navigate fragmented systems or unaffordable costs. In this context, people-centered, equity-driven approaches are critical.[6,7]

Embracing the theme means:[7-12]

- Improving early detection through culturally appropriate outreach and education, delivered in the languages and channels people trust.
- Reducing financial toxicity by expanding coverage, transparent pricing, patient navigation, and employer policies that protect income and jobs.
- Integrating mental health into routine care, recognizing anxiety, depression, trauma, and caregiver stress as core clinical concerns.
- Leveraging technology thoughtfully, ensuring telehealth and digital tools connect, not exclude, people with limited connectivity or digital literacy.
- Championing palliative care as a right, not a last resort—available early, alongside curative or life-prolonging treatments.
- Focusing on survivorship: rehabilitation, return-to-work programs, fertility and sexual health services, and long-term follow-up for late effects.

In short, centering people leads to better engagement, better adherence, better outcomes—and a more humane system for all.

From Disease-Centered to People-Centered: A Necessary Shift

Traditional cancer systems tend to be organized around diagnoses, protocols, and facilities—important foundations that enable consistent, evidence-based care. Yet these structures can inadvertently marginalize the personal, social, and cultural factors that determine whether care is accessible, acceptable, and effective for each person. A people-centered approach rebalances that equation. It integrates the science of medicine with the art of listening, empathy, and co-design.[13]

A people-centered cancer system:[7-9,13-15]

- Sees the whole person, not just the tumor: their values, beliefs, family roles, work obligations, and goals for care.
- Plans with, not for the patient: shared decision-making that respects autonomy and preferences.
- Coordinates across the continuum: prevention, screening, diagnosis, treatment, rehabilitation, palliative care, and survivorship support are linked and navigable.
- Respects diversity: care is culturally sensitive and linguistically appropriate; it addresses gender, age, disability, and socio-economic contexts.
- Builds trust and compassion: communication is clear, honest, and supportive; mental health and social support are embedded, not optional.
- Focuses on equity: addresses barriers like distance, cost, stigma, legal status, and digital divides that prevent people from getting timely help.

This is not a rejection of medical excellence. It is an expansion of it—where compassion, lived experience, and clinical expertise reinforce each other.

What People-Centered Care Looks Like in Practice[16]

Turning principle into practice requires both mindset shifts and practical tools. Here is a patient-centered communication framework organizations can adopt (**Figure 1**): The six core functions of patient-clinician communication overlap and interact to produce communication that can affect important health outcomes.

- **Exchanging information** emphasizes the importance of recognizing patients' information needs, integrating clinical information with the patient's illness representations, acknowledging both the content and process of information exchange, recognizing that disease-related information now is more available through the Internet, communicating prognostic information accurately while also providing hope, and overcoming barriers related to low health literacy and poor understanding of statistical information.
- **Responding to emotions** requires clinicians to elicit patients' emotional distress; communicate an understanding of the patient's emotions to him or her; and respond with legitimation, validation, empathy, and support.

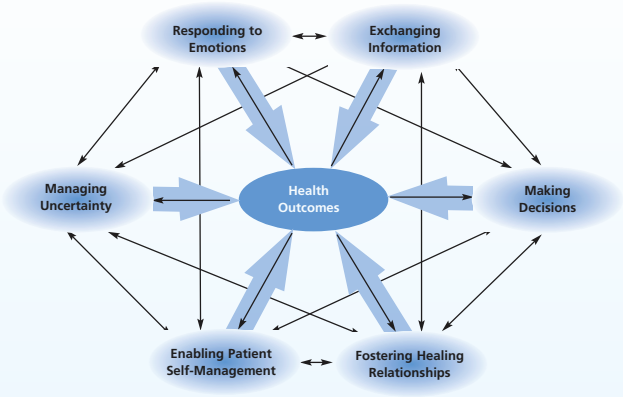


Figure 1: National Cancer Institute framework for patient-centered communication[16]

- **Managing uncertainty** emphasizes that uncertainty often cannot be eliminated but can be managed by providing information, support, and cognitive strategies to help patients and families deal more effectively with the anxiety related to uncertainty.
- **Making decisions** involves consideration of both the active involvement of the patient and family in the information exchange and deliberation stages of the decision-making process and the identification of the person responsible for the final decision.
- Lastly, **enabling patient self-management** involves advocacy for the patient, including navigating the patient through the health care system; supporting patient autonomy; and providing guidance, skills, and access to resources.

The Roles We All Play

Creating people-centered cancer care is a shared responsibility. Healthcare professionals can champion empathetic communication, inter-disciplinary teamwork, and personalized plans. Healthcare organizations can resource navigation services, embed mental health, and measure what matters to patients. Policymakers can expand coverage, protect employment rights, and fund community-based prevention and early detection. Employers can offer flexible leave, accommodations, and stigma-free return-to-work policies. Researchers and innovators can include diverse populations in trials and co-design tools with end users. Educators and media can reduce stigma and spread accurate, accessible information. Communities and faith-based groups can provide practical support, connection, and trust.

Additionally, individuals—with or without a direct link to cancer—can contribute by learning, listening, donating, volunteering, advocating, and checking in on neighbors and colleagues. Small acts add up. When we look beyond the disease and truly see the person, care becomes not only more compassionate—it becomes more effective.[1]

Stories as a Catalyst for Change

Stories humanize data. Behind every diagnosis is a life story. Some are stories of grief, as individuals and families face uncertainty or loss. Others are stories of pain, both physical and emotional, that require skill and sensitivity to manage. Many are stories of healing and resilience, charting pathways through treatment, adaptation, and newfound strengths. Furthermore, numerous stories are rooted in love—communities rallying, caregivers holding steady, friends showing up, workplaces accommodating, and health professionals offering care beyond the call of duty.

On this World Cancer Day, consider whose story you can uplift: a survivor's return to joy, a caregiver's quiet strength, a clinician's steadfast presence, or a community's collective response. Stories connect us—united by what is unique in each person.

Conclusion

As World Cancer Day 2026 approaches, "United by Unique" invites us to transform how we think about and deliver cancer care. It asks us to place people at the center, to recognize that behind every diagnosis is a singular story that deserves respect, empathy, and partnership. A people-centered approach is not an optional enhancement; it is the pathway to better outcomes, greater equity, and dignified care. When we unite—patients and survivors, families and clinicians, employers and policymakers, researchers and advocates—we create systems that look beyond the disease and truly see the person. In doing so, we honor every story and move closer to a world where compassionate, personalized, and equitable cancer care is a reality for all.

United by our shared humanity, strengthened by our unique journeys—this is how we change the future of cancer care.

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by Dr. Feng Xue

Tai Chi vs CBT-I: Can Ancient Wisdom Rival Modern Therapy for Insomnia?

Chronic insomnia is a widespread condition among middle-aged and older adults, yet access to first-line treatment—Cognitive Behavioral Therapy for Insomnia (CBT-I)—remains limited due to cost and therapist availability. This article examines findings from a large randomized non-inferiority trial comparing Tai Chi, a traditional mind-body practice, with CBT-I in adults aged 50 and above. While Tai Chi was less effective than CBT-I immediately after the three-month intervention, it achieved non-inferior long-term improvements at the 12-month follow-up. Both groups demonstrated significant enhancements in insomnia severity, sleep quality, mental wellbeing, and physical functioning, with no adverse events reported. The results highlight Tai Chi as an accessible, low-cost, and sustainable alternative for long-term management of chronic insomnia in aging populations.[1]

The Silent Epidemic of Sleeplessness

Chronic insomnia is one of the most prevalent sleep disorders among middle-aged and older adults, affecting up to 50% of individuals in Hong Kong and between 4% to 22% globally.[2,3] Beyond the nightly struggle to fall asleep, insomnia carries severe consequences—heightened risks of cardiovascular disease, mental health disorders, cognitive decline, and even increased mortality.[4] The economic toll is staggering, with annual costs in the United States alone estimated at $150 billion.[5]

The first line treatment for insomnia is CBT-I, praised for its efficacy and minimal side effects.[6] Yet, CBT-I faces barriers: high costs, limited availability of trained therapists, and low referral rates.[7,8] Data from 12 European countries indicate that only 4-10% of patients are prescribed nonpharmacological insomnia treatments such as CBT-I.[9] This accessibility gap has sparked interest in alternative, cost-effective interventions—here comes Tai Chi, a centuries-old mind-body practice.[10,11]

Putting Tai Chi to the Test

Researchers from Hong Kong, Macau, Europe and America conducted a randomized, assessor-blinded, non-inferiority trial in a single research site in Hong Kong to compare Tai Chi with CBT-I for treating chronic insomnia in adults aged 50 and above. The study enrolled 200 participants, all diagnosed with chronic insomnia under the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) criteria.[1]

Intervention Details[1]

- Tai Chi group: Practiced the 24-form Yang style twice weekly for three months.
- CBT-I group: Received standard CBT-I sessions twice weekly covering sleep education, stimulus control, sleep restriction, relaxation training, and cognitive therapy.

Both interventions consisted of 24 one-hour sessions over three months, followed by a 12-month post-intervention follow-up.

Outcome measure

Primary Outcome[1,12]

The primary measure was the Insomnia Severity Index (ISI), assessed at 3 months (post-intervention) and 15 months (12-month follow-up). A non-inferiority margin of 4 points on the ISI was set, representing half of the minimally important difference.

The per protocol analysis showed that at 3 months, CBT-I outperformed Tai Chi:

- CBT-I: ISI reduction of 11.19 points
- Tai Chi: ISI reduction of 6.67 points
- Difference: 4.52 points (Tai Chi deemed inferior)

However, the story changed at 15 months:

- CBT-I: ISI reduction of 10.18 points
- Tai Chi: ISI reduction of 9.51 points
- Difference: 0.68 points (Tai Chi deemed non-inferior)

This suggests that while CBT-I delivers faster relief, Tai Chi catches up over time, offering comparable long-term benefits. The results of the sensitivity analyses on the primary outcome were consistent with the primary analysis (**Figure 1**).

Secondary Outcomes and Safety Profile[1]

- Remission Rates: At 3 months, CBT-I showed clear advantage (83.3% vs 56.1%, p<0.001). By 15 months, the rates were similar (63.4% vs 76.5%, p=0.067).
- Treatment Response: CBT-I dominated early (77.4% vs 43.9%, p<0.001), but differences narrowed at follow-up (73.2% vs 62.4%, p=0.137).
- No adverse events were reported in either group.

Why Does Tai Chi Work?

Tai Chi is more than gentle movement—it's a holistic practice integrating physical, psychological, and emotional components. Research suggests Tai Chi reduces stress, depressive symptoms, and cognitive hyperarousal, all key drivers of insomnia.[13,14] In contrast, CBT-I primarily targets dysfunctional sleep-related beliefs, addressing specific maladaptive patterns that sustain insomnia.[15]

Interestingly, Tai Chi may also influence inflammatory pathways. Previous trials show Tai Chi reduces systemic and cellular inflammation, which is increasingly recognized as a contributor to chronic insomnia.[16]

Advantages of Tai Chi Over CBT-I[1,17,18]

- Accessibility: Tai Chi requires no specialized therapists and can be practiced in community settings.
- Affordability: Minimal cost compared to structured CBT-I sessions.
- Cultural Appeal: Particularly suitable for older adults, widely accepted in Asian communities and growing popularity in western countries.
- Sustainability: Participants were more likely to continue Tai Chi after intervention (36.5% vs 15.9% for CBT-I self-practice).

Limitations and Considerations

The study was conducted in Hong Kong, with 77.5% of participants aged 60 years and older, which may limit generalizability to younger populations or different cultural contexts. Additionally, future studies are warranted to regularly assess adherence to Tai Chi during the post-intervention follow-up period to capture the full tai chi practice behavior.[1]

Implications for Healthcare

Given the high cost and limited reach of CBT-I, Tai Chi emerges as a promising alternative for long-term insomnia management. Its scalability and cultural adaptability make it an attractive option for public health strategies, especially in aging societies.[17,18]

Bridging Tradition and Science

This landmark trial demonstrates that while Tai Chi may not match CBT-I's rapid efficacy, it achieves comparable long-term outcomes without adverse effects. For millions struggling with chronic insomnia—and for healthcare systems burdened by its costs—Tai Chi offers a practical, low-cost, and sustainable solution.

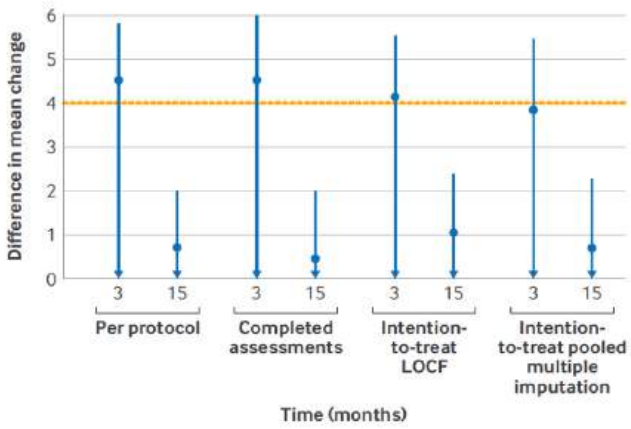

Figure 1: *Primary outcome (per protocol analysis): non-inferiority analysis for ISI at 3 and 15 months in Tai Chi and CBT-I groups.*[1] *Sensitivity analyses: completed assessments, intention-to-treat last observation carried forward (LOCF), and intention-to-treat pooled multiple imputation*

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by Dr. Feng Xue

Even Small Lifestyle Changes Could Help You Live Longer and Better

Sleep, physical activity, and nutrition are foundational, modifiable behaviors that shape both how long people live (lifespan) and how long they live free of major chronic disease (healthspan).[1,2] Yet these behaviors are often studied and targeted one at a time.[3,4] Here we share a prospective cohort study of 59,078 UK Biobank participants, which examined how combined improvements across these three domains—collectively termed SPAN (Sleep, Physical Activity, and Nutrition)—relate to gains in lifespan and healthspan using device-measured sleep and moderate-to-vigorous physical activity (MVPA), alongside a validated diet quality score (DQS).[5] Over a median follow-up of 8.1 years, the study estimated life expectancy and disease-free life expectancy across joint SPAN categories and a composite SPAN score. The findings suggest that while large changes in any single behavior may be required to achieve meaningful benefits, small concurrent improvements across all three can be associated with substantial gains, including an estimated ~1 extra year of lifespan from as little as +5 minutes/day sleep, +1.9 minutes/day MVPA, and +5 DQS points. More sizable combined changes were associated with several additional years of healthspan.[5] These results support a pragmatic public health message: modest, multi-behavior "micro-changes" may be more feasible—and still meaningful—than major changes in one domain alone.

Why Do Researchers Study Sleep, Activity, and Nutrition Together?

Sleep, physical activity, and diet are tightly interdependent in real life. Poor sleep can dysregulate appetite and energy balance, potentially increasing caloric intake; it can also reduce energy and motivation for movement. Diet composition can influence sleep quality, and physical activity can improve sleep timing and depth. The study positions SPAN as a system of interacting behaviors rather than three isolated exposures, arguing that a single-behavior research and policy mindset may miss synergistic effects and undervalue small, coordinated improvements.[6]

This matters because many countries have seen lifespan rise while healthspan stagnates or declines—meaning more years lived with chronic conditions.[1,2] From a prevention standpoint, delaying onset of major diseases such as cardiovascular disease (CVD), cancer, type 2 diabetes, chronic obstructive pulmonary disease (COPD), and dementia is central to improving quality of life and reducing healthcare burden.[7] The study therefore focused on both all-cause mortality (lifespan) and disease-free life expectancy (healthspan) across those five conditions.[5]

Study Design

Cohort and Measurements[5,8]

The analysis used 59,078 adults from the UK Biobank accelerometry sub-study (recruited 2006–2010; median age ~64 years). Between 2013 and 2015, participants wore a wrist accelerometer for 7 days, enabling device-based estimates of:

- Sleep duration (hours/day) via a validated wrist-tilt algorithm
- MVPA (minutes/day) using a validated machine-learning classifier
- Diet was assessed earlier at baseline using a food-frequency questionnaire to compute a DQS (0–100) covering key food groups (vegetables, fruits, fish, dairy, whole grains, oils, refined grains, processed/unprocessed meats, and sugar-sweetened beverages).

Outcomes and Follow-up[5,6,9]

Over a median follow-up of 8.1 years, the cohort accumulated: 2458 deaths, 9996 CVD, 7681 cancers, 2971 type 2 diabetes, 1540 COPD, and 508 dementia events. Lifespan and healthspan were estimated using life-table methods and hazard ratio-adjusted rates from multivariable models.

The researchers grouped each SPAN behavior into tertiles and evaluated 27 combinations (3 sleep × 3 MVPA × 3 DQS). They also created a composite SPAN score (0–100) to quantify incremental "dose" changes needed for specific gains.

The tertile ranges were practical and interpretable:

- Sleep: low 4.8–7.2 h/day; medium 7.2–8.0; high 8.0–9.4
- MVPA: low 5–23 min/day; medium 23–42; high 42–103
- Diet quality (DQS): low 32.5–50.0; medium 50.0–57.5; high 57.5–72.5

Notably, the "medium MVPA" range begins just above ~22 minutes/day, aligning closely with common guideline-equivalent thresholds.

Key Findings[5]

Compared with the least favorable tertiles, the most favorable SPAN pattern (notably high MVPA, moderate sleep, and high DQS) was associated with:

- +9.35 years of lifespan (95% confidence interval [CI] 6.67–11.63)
- +9.46 years of healthspan (95% CI 5.45–13.61)

This is a striking finding: the model-based estimates suggest that optimal combined behaviors correspond to nearly a decade more life and a decade more life free of major chronic disease (**Figure 1**).

Across joint categories, moving into the moderate MVPA group (>22 min/day) was a visible "turning point" for gains, even when sleep and diet were not optimal. For example, moderate MVPA + moderate sleep + high DQS corresponded to about +7.00 years lifespan and +6.32 years healthspan relative to the lowest tertiles.

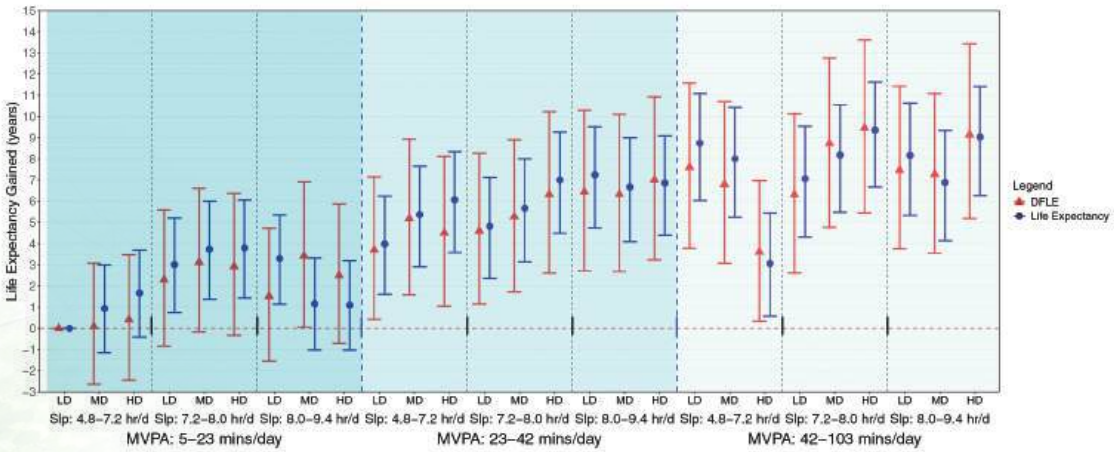

Figure 1: Multivariable-adjusted lifespan and healthspan associated with joint sleep, physical activity, and nutrition exposures.[5] DFLE, Disease-Free Life Expectancy; HD, High Diet Quality; LD, Low Diet Quality; MD, Medium Diet Quality; Slp, Sleep

Tiny Concurrent Changes, Meaningful Gains[5]

A central contribution of the study is translating statistical associations into minimum combined "doses" of change required for meaningful gains. Compared with the 5th percentile baseline for all three behaviors, the study estimated that ~1 additional year of lifespan was associated with +5 minutes/day sleep, +1.9 minutes/day MVPA, and +5 points in DQS (examples given: ~½ serving of vegetables/day or ~1.5 servings of whole grains/day). The practical message is powerful: for lifespan, small shifts across multiple behaviors may add up.

Bigger (But Still Plausible) Combined Change for Healthspan Gains[5]

Healthspan required larger changes before estimates became statistically clear. The study reported that ~4 additional years of healthspan were associated with +24 minutes/day sleep, +3.7 minutes/day MVPA, and +23 DQS points (example pattern: +1 cup vegetables/day, +1 serving whole grains/day, and +2 servings fish/week). In other words, preventing or delaying major chronic disease onset (not just mortality) appears to demand more substantial combined improvements.

Do the Behaviors Work Synergistically?[5]

The researchers tested whether the combined effect of SPAN exceeds what you would expect from simply adding the parts (interaction on an additive scale). They found:

- Modest positive synergy for all-cause mortality (evidence consistent with "more than additive" benefit)
- No clear synergy for overall healthspan, though some borderline indications appeared for cancer risk

This nuance matters: even if synergy is limited for disease-free life expectancy, the combined approach still lowered the "required dose" of change relative to pursuing one behavior alone.

Practical Takeaways: A "Micro-Change" SPAN Strategy

While the study does not prescribe an intervention, it implies a pragmatic approach:

- Aim for MVPA momentum first. Moving from low to moderate MVPA (>~22 min/day) corresponded to notable gains across combinations.
- Add small sleep improvements toward ~7.2–8.0 hours/day. Sleep showed an inverted U-shaped pattern with an apparent "sweet spot" around mid–7 hours.
- Nudge diet quality upward with concrete swaps. Even if diet alone looked modest here, combined improvements mattered; examples included more vegetables/whole grains and more fish.
- Combine changes rather than "all-in" on one. The key thesis is feasibility: small coordinated steps may be easier to sustain and still meaningful.

Of note, due to selection bias, residual confounding, and its observational design, the study cannot establish causality and has limited generalizability.

Conclusion

This population cohort study provides an unusually actionable translation of lifestyle epidemiology: it estimates how small, combined changes in sleep, physical activity, and diet quality relate to gains in both lifespan and healthspan. The standout message is that the "minimum effective change" may be far smaller when behaviors improve together: roughly +5 minutes/day sleep, +2 minutes/day MVPA, and a +5-point diet quality improvement were associated with ~1 extra year of lifespan. More substantial combined improvements were associated with multiple additional years free of major chronic disease. Although observational and model-based, the results support a practical public health direction: instead of demanding major transformation in one domain, health authorities could encourage achievable micro-changes across the SPAN triad, potentially leveraging behavioral interdependence to enhance adherence and population impact.

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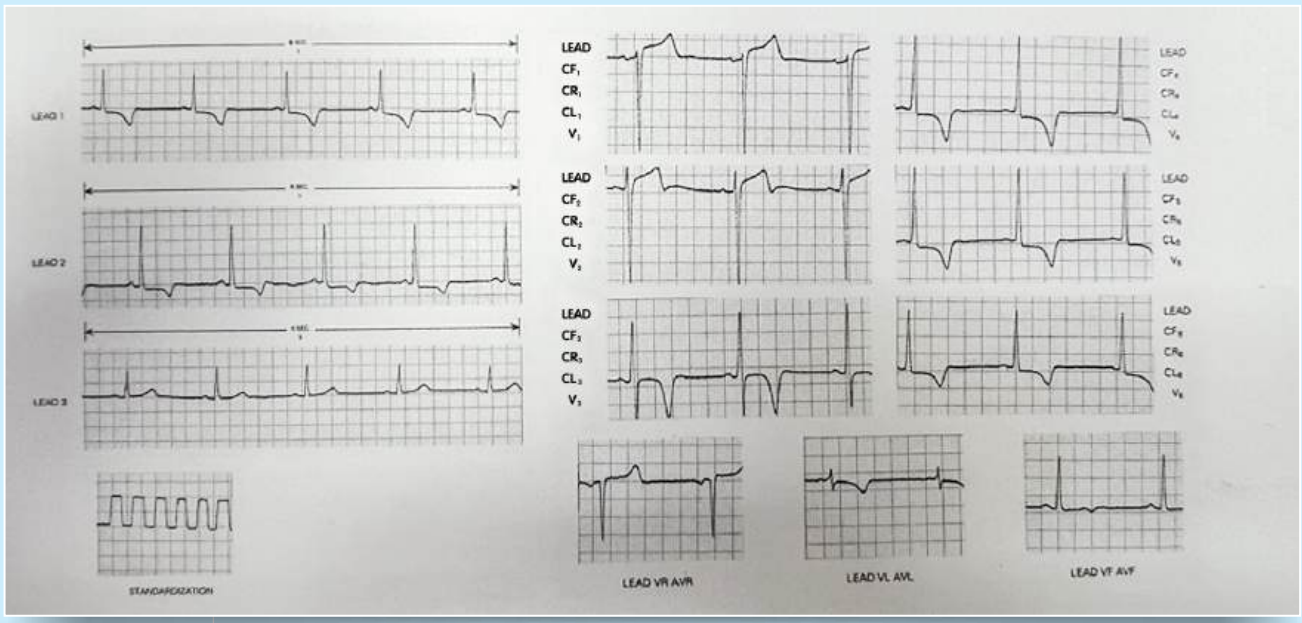
ECG CME FEBRUARY 2026 (0.5 CME POINTS)

Dr. Pun Chiu On, Specialist in Cardiology

History:

This 38 year old man came for routine medical check up. His past health was good. Blood pressure was 125/80 mmHg. This is his ECG. *Please note that the voltage of V3-V6 was half.



Question: **What is the ECG diagnosis?**

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-FEBRUARY-2026***

SCAN ME

Answer to December 2025 Issue's CME

ECG diagnosis: Complete left bundle branch block.

Reason for the ECG diagnosis:

- QRS complex is widened to 0.14 seconds (normal <0.12).
- The QRS complexes at leads I, II, aVL, V5-V6 are slightly notched and showed somewhat "M" shape pattern.
- Absence of septal Q wave in leads V4-V6.
- Absence of R wave in V1.
- Please note that the QRS axis is usually normal in left bundle branch block. Sometimes the axis is indeterminate. The axis of this ECG is +15° (normal axis -30° to +90°).
- Non-specific ST segment depression and T wave inversion may occur at left side leads (I, aVL, V6).

Possible aetiology:

Always indicate underlying organic heart disease.

- Ischemic heart disease (commonest).
- Valvular heart disease in particular aortic valve disease.
- Cardiomyopathy.
- Congenital heart diseases.
- Myocarditis.

Significance:

It depends on the underlying etiology.

Principle of management:

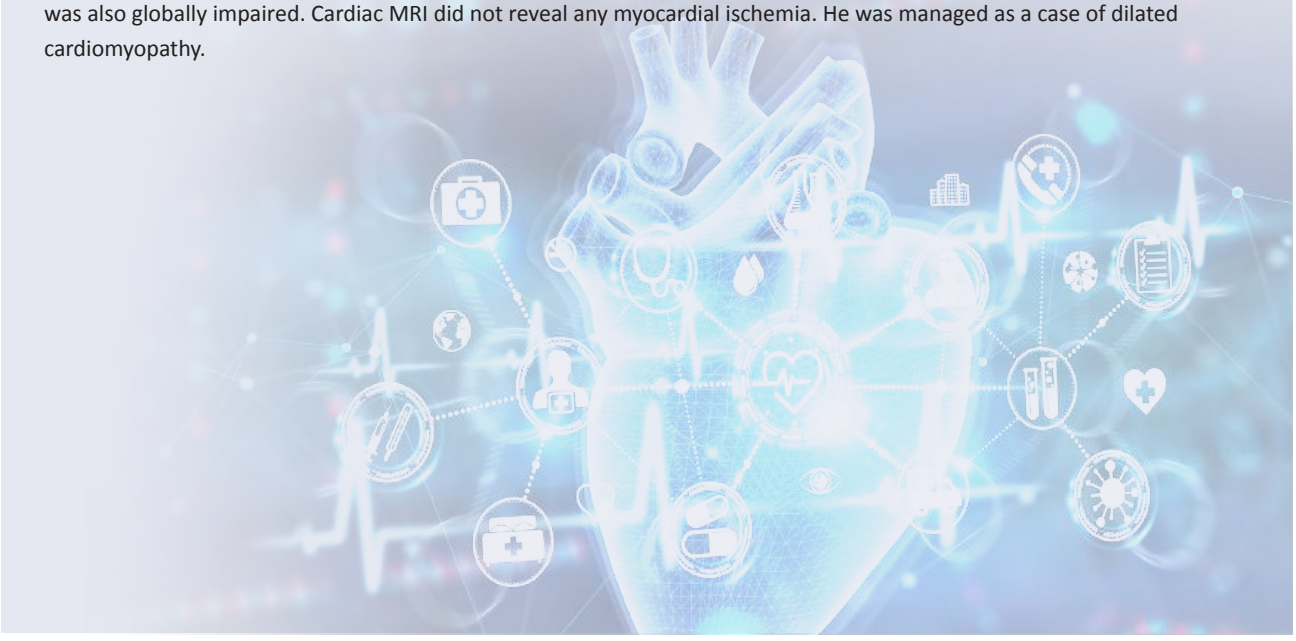
Look for underlying heart disease from history and physical examination. If in doubt, further simple non-invasive investigations would include chest x-ray, echocardiography.

Exercise stress test is not indicated because of false positive result in complete left bundle branch block. If ischemia heart disease is suspected, consider cardiac magnetic resonance imaging (cardiac MRI) which is non-invasive and diagnostic, or CT coronary angiography.

Treat underlying organic heart disease if found.

Management of this patient:

Echocardiography for this patient showed enlarged left atrium, left ventricle and right ventricle. Left ventricular contraction was also globally impaired. Cardiac MRI did not reveal any myocardial ischemia. He was managed as a case of dilated cardiomyopathy.



by Michelle Lee

On-the-Pulse

Psychiatry & Addiction Medicine

Risk of Gambling-Related Suicidal Ideation

Among 2,800 help-seekers for gambling-related problems in Finland, women demonstrated significantly higher rates of suicidal ideation compared to men (25.5% versus 16.4%), with gambling-related debts and inadequate social support identified as critical risk factors for both sexes. Analysis using logistic regression revealed that at-risk alcohol use independently elevated suicidal ideation risk only in women, whereas both genders showed similar vulnerability to gambling indebtedness and social disconnection. Notably, the protective effect of social support proved stronger for men, who exhibited substantially higher odds ratios (2.63) compared to women. These gender-differentiated associations emphasise the necessity for sex-specific prevention and intervention strategies tailored to address distinct vulnerability pathways in gambling harm reduction programs.[1]

Burn Injury

Cholestasis After Burn Injury

Burn-associated cholestasis (BAC) is a common complication following severe burn injuries, characterised by elevated liver enzymes and bilirubin levels. A study examined the clinical significance and prognostic value of cholestasis patterns in burn patients admitted to intensive care units. The researchers identified three distinct categories: BAC-A (elevated alkaline phosphatase and gamma-glutamyltransferase without hyperbilirubinemia), BAC-B (elevated enzymes with elevated bilirubin), and BAC-C (hyperbilirubinemia alone). Risk factors independently associated with BAC development included higher burn severity scores, ketamine use, mechanical ventilation, and parenteral nutrition. Importantly, bilirubin trajectories emerged as early predictors of mortality risk, with dynamic changes in cholestasis parameters providing critical prognostic information. These findings highlight that cholestasis in burn patients is highly dynamic rather than static, and monitoring bilirubin dynamics could guide clinical decision-making and identify high-risk patients requiring intensive intervention.[2]

Neurology

Long-Term Exposure to Air Pollution and Risk of Motor Neuron Disease

A landmark case-control study examined whether prolonged exposure to air pollution is associated with the risk and progression of motor neuron disease (MND), commonly known as ALS. The research found that long-term exposure to particulate matter and other air pollutants was significantly linked to an elevated risk of developing motor neuron disease. Beyond disease onset, the study demonstrated that individuals with elevated cumulative air pollution exposure experienced accelerated disease progression, suggesting air pollution may contribute not only to ALS incidence but also to how rapidly the condition advances. These findings underscore the environmental determinants of neurodegeneration and highlight air quality as a potentially modifiable risk factor for motor neuron disease. The results have implications for public health policy, occupational safety guidelines, and patient counselling regarding environmental exposures and their relationship to neurodegenerative disease progression.[3]

Diabetology

Empagliflozin in HNF1A-related maturity-onset diabetes of the young

A randomised controlled trial evaluated the glucose-lowering efficacy of empagliflozin, an SGLT2 inhibitor, as an adjunctive treatment in patients with HNF1A-related maturity-onset diabetes of the young (HNF1A-MODY), a rare monogenic form of diabetes. Over a 4-week intervention period, patients receiving empagliflozin alongside existing glucose-lowering therapies demonstrated significantly improved glycemic control measured by continuous glucose monitoring compared to placebo. Key secondary endpoints included reductions in 24-hour urinary glucose excretion, elevated estimated renal glucose thresholds, and lower fasting plasma glucose levels, with no substantial increase in hypoglycemic episodes or adverse events reported. The findings support empagliflozin's clinical relevance as a second-line or third-line therapeutic option even in HNF1A-MODY patients, despite the condition's potentially reduced SGLT2 expression, establishing evidence for SGLT2 inhibitor use in this specific genetic diabetes subtype.[4]

Psychiatry

Methylphenidate Use in ADHD Children's Growth

Children diagnosed with ADHD, particularly those receiving long-term methylphenidate treatment, demonstrated higher body mass index (BMI) and reduced height at adulthood compared to individuals without ADHD. This matched cohort study examined growth trajectories across early childhood through adulthood, controlling for socioeconomic factors, dietary patterns, and physical activity levels. Findings revealed that methylphenidate exposure was independently associated with increased adiposity and altered body composition, even when accounting for baseline ADHD severity. The mechanism underlying this association remains unclear, potentially involving appetite suppression during medication periods followed by compensatory weight gain during off-medication hours, metabolic alterations, or behavioural responses to dopaminergic changes. The average height differential between treated and untreated ADHD cohorts was modest (approximately 0.5 cm), while BMI differences were more pronounced. These findings highlight the importance of monitoring growth and metabolic parameters in children receiving stimulant medications for ADHD and suggest consideration of individual risk-benefit profiles when initiating long-term pharmaceutical treatment.[5]

Cardiology

Effectiveness and Safety of Statins in Type 2 Diabetes According to Baseline Cardiovascular Risk

A target trial emulation study analysed 10-year outcomes for statin initiation among type 2 diabetes patients stratified by cardiovascular risk using UK primary care data. For low-risk individuals, statins reduced all-cause mortality by 0.53% and major cardiovascular disease events by 0.83% over 10 years. Among moderate-risk and high-risk groups, absolute risk reductions were substantially larger, with relative risk ratios of 0.78-0.85 across risk strata. Notably, myopathy risk increased minimally only in the moderate-risk stratum, while liver dysfunction showed no significant elevation across any risk category. These findings support statin use for primary cardiovascular prevention across the entire spectrum of type 2 diabetes patients, including those with predicted low 10-year cardiovascular risk, challenging existing guidelines that restrict statins to higher-risk individuals.[6]

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

References

1. Marionneau V, Havuaho S, Wall H. Gender-specific risk factors for gambling-related suicidal ideation: Evidence from a help-seeking population. Addictive Behaviors. 2026;175;108616. **2.** Semmler L, Semmler G, Langa A, et al. Characterisation and Prognostic Implication of Cholestasis After Burn Injury. Aliment Pharmacol Ther. 2026;0:1-11. **3.** Wu J, Pyko A, Chourpiliadis C, et al. Long-Term Exposure to Air Pollution and Risk and Prognosis of Motor Neuron Disease. JAMA Neurol. 2026:e255379. **4.** Maagensen H, Høyerup SO, Jensen JS, et al. Empagliflozin in HNF1A-MODY (MODY3)-a Randomized, Double-Blind, Placebo-Controlled, Crossover Trial. Diabetes Care. 2026:dc252572. **5.** Song J, Park SJ, Yu J, et al. ADHD and Methylphenidate Use in Prepubertal Children and BMI and Height at Adulthood. JAMA Netw Open. 2026;9(1):e2552019. **6.** Yan VKC, Blais JE, Gamble JM, et al. Effectiveness and Safety of Statins in Type 2 Diabetes According to Baseline Cardiovascular Risk : A Target Trial Emulation Study. Ann Intern Med. 2025. doi: 10.7326/ANNALS-25-00662.

Infectious Disease:

EMBLAVEO®

(aztreonam and avibactam)

PFIZER

HK Reg. No. HK-68891 (03 Nov, 2025)

Composition[1]:

- Each vial contains 1.5 g aztreonam and avibactam sodium equivalent to 0.5 g avibactam
- After reconstitution, 1 mL of solution contains 131.2 mg of aztreonam and 43.7 mg of avibactam

Indication[1]:

Emblaveo® is indicated for the treatment of the following infections in adult patients:

- Complicated intra-abdominal infection (cIAI)
- Hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)
- Complicated urinary tract infection (cUTI), including pyelonephritis

Emblaveo® is also indicated for the treatment of infections due to aerobic Gram-negative organisms in adult patients with limited treatment options

Rheumatology:

SPEVIGO®

(spesolimab)

BOEHRINGER INGELHEIM

HK Reg. No. HK-68915 (03 Dec, 2025)

Composition[2]:

For subcutaneous use:

- Injection: 150 mg/mL in a single-dose prefilled syringe

Indication[2]:

SPEVIGO® is an interleukin-36 receptor antagonist indicated for the treatment of generalized pustular psoriasis (GPP) in adults and pediatric patients 12 years of age and older and weighing at least 40 kg

Psychiatry:

ZOLOFT®

(sertraline, as hydrochloride)

VIATRIS

HK Reg. No. HK-68926 (09 Dec, 2025)

Composition[3]:

- ZOLOFT® is available in 100 mg tablets, along with other dosage forms

Indication[3]:

ZOLOFT® is a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of:

- Major depressive disorder (MDD)
- Obsessive-compulsive disorder (OCD)
- Panic disorder (PD)
- Post-traumatic stress disorder (PTSD)
- Social anxiety disorder (SAD)
- Premenstrual dysphoric disorder (PMDD)

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.

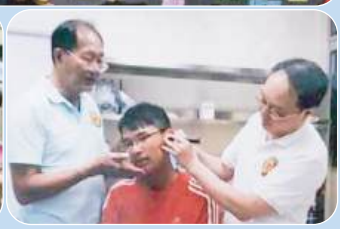
In future, the HKDU will continue humbly listening and keep on improving in our role as the channel between local medical doctors and our society.

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

Oncology:

HYCAMCORD®

(topotecan, as hydrochloride)

JACOBSON

HK Reg. No. HK-68935 (11 Dec, 2025)

Composition[4]:

- Each vial contains 4 mg topotecan (powder for concentrate for solution for infusion)
- The total content of active substance in the vial provides 1 mg per mL of active substance when reconstituted as recommended

Indication[4]:

HYCAMCORD® monotherapy is indicated for the treatment of:

- patients with metastatic carcinoma of the ovary after failure of first-line or subsequent therapy
- patients with relapsed small cell lung cancer (SCLC) for whom re-treatment with the first-line regimen is not considered appropriate

HYCAMCORD® in combination with cisplatin is indicated for patients with carcinoma of the cervix recurrent after radiotherapy and for patients with Stage IVB disease. Patients with prior exposure to cisplatin require a sustained treatment-free interval to justify treatment with the combination

References

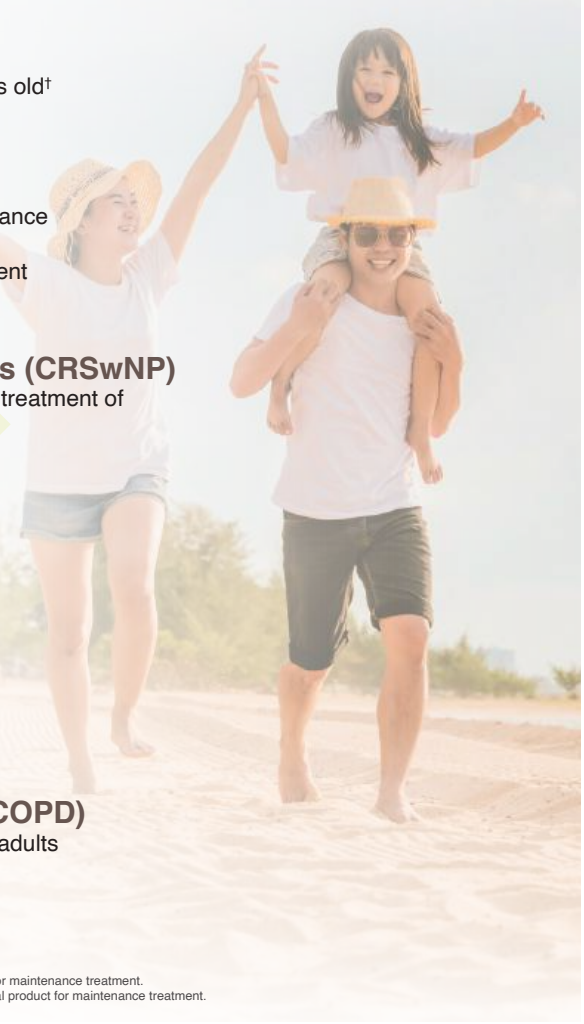
1. EMA. Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/emblaveo-epar-product-information_en.pdf. [Accessed 23 December 2025]. **2.** FDA. Highlights of Prescribing Information. March 2024. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761244s003lbl.pdf. [Accessed 23 December 2025]. **3.** FDA. Highlights of Prescribing Information. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/019839s74s86s87_20990s35s44s45lbl.pdf. [Accessed 23 December 2025]. **4.** EMA. Summary of Product Characteristics. Available from: https://www.ema.europa.eu/en/documents/product-information/hycamtin-epar-product-information_en.pdf. [Accessed 23 December 2025].

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

One Target, Dual Action, Six Indications

DUPIXENT targets IL-4Ra with dual action on both IL-4 & IL-13 to reduce Type 2 inflammation[1,2]

DUPIXENT - your versatile biologic that targets six conditions[3]



Atopic Dermatitis (AD)
- Moderate-to-severe AD in adults and adolescents ≥12 years old†
- Severe AD in children 6 months to 11 years old†

6+ months

Asthma
- In adults and adolescents ≥12 years old as add-on maintenance treatment for severe asthma with Type 2 inflammation*
- In children 6 to 11 years old as add-on maintenance treatment for severe asthma with Type 2 inflammation^

6+ years

Chronic rhinosinusitis with nasal polyposis (CRSwNP)
- As an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP#

18+ years

Prurigo Nodularis (PN)
- Moderate-to-severe PN in adults who are candidates for systemic therapy

18+ years

Eosinophilic Esophagitis (EoE)
- In adults and adolescents ≥12 years old weighing ≥40 kg‡

12+ years

Newly approved

Chronic Obstructive Pulmonary Disease (COPD)
- As add-on maintenance treatment with other medicines for adults with uncontrolled COPD§

18+ years

† Candidates for systemic therapy
* Characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment.
^ Characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with medium to high dose ICS plus another medicinal product for maintenance treatment.
# For whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.
‡ Those who are inadequately controlled by, are intolerant to, or who are not candidates for conventional medicinal therapy.
§ Characterised by raised blood eosinophils, on a combination of an inhaled corticosteroid (ICS), a long acting beta2-agonist (LABA), and a long-acting muscarinic antagonist (LAMA), or on a combination of a LABA and a LAMA if ICS is not appropriate.

Abbreviations: AD=atopic dermatitis; COPD = chronic obstructive pulmonary disease; CRSwNP= chronic rhinosinusitis with nasal polyps; EoE= eosinophilic esophagitis; FeNO=fractional exhaled nitric oxide; ICS=inhaled corticosteroids; LABA = long acting beta2-agonist; LAMA = long acting muscarinic antagonist; PN=prurigo nodularis.

References:
1. Guttman-Yassky E, et al. J Allergy Clin Immunol. 2019;143(1):155-172. 2. Gandhi NA, et al. Nat Rev Drug Discov. 2016;15(1):35-50 3.DUPIXENT® Hong Kong Prescribing Information

Presentation: Dupilumab solution for injection in a pre-filled syringe with needle shield. **Indications:** Atopic Dermatitis (AD): Moderate-to-severe AD in adults and adolescents ≥12 years who are candidates for systemic therapy; severe atopic dermatitis in children 6 months to 11 years old who are candidates for systemic therapy. Asthma: In adults and adolescents ≥12 years as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment. In children 6 to 11 years old as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with medium to high dose ICS plus another medicinal product for maintenance treatment. For 300 mg only – Chronic rhinosinusitis with nasal polyposis (CRSwNP): As an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control. Prurigo Nodularis (PN): Moderate-to-severe PN in adults who are candidates for systemic therapy. Eosinophilic esophagitis (EoE): In adults and adolescents ≥12 years, weighing ≥40 kg, who are inadequately controlled by, are intolerant to, or who are not candidates for conventional medicinal therapy. Chronic obstructive pulmonary disease (COPD): In adults as add-on maintenance treatment for uncontrolled COPD characterised by raised blood eosinophils on a combination of ICS, LABA, and LAMA, or on a combination of LABA and LAMA if ICS is not appropriate. **Dosage & Administration:** Subcutaneous injection. AD adults: Initial dose of 600 mg (two 300 mg injections), followed by 300 mg Q2W. AD adolescents (12-17y/o): Body weight <60 kg- initial dose of 400 mg (two 200 mg injections), followed by 200 mg Q2W. Body weight ≥60 kg- same dosage as adults. AD children (6-11y/o): Body weight 15kg-<60 kg- initial dose of 300 mg on Day 1 follow by 300 mg on Day 15, then 300mg Q4W. Body weight ≥60 kg- same dosage as adults. * The dose may be increased to 200 mg Q2W in patients with body weight of 15 kg-< 60 kg based on physician's assessment. AD children (6 months-5y/o): Body weight 5kg-<15 kg- initial dose of 200 mg, then 200 mg Q4W. Body weight 15kg-<30 kg- initial dose of 300 mg, then 300 mg Q4W. Dupilumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, e.g. face, neck, intertriginous and genital areas. Consider discontinuing treatment in patients who have shown no response after 16 weeks. Asthma adults and adolescents: Initial dose of 400 mg, followed by 200 mg Q2W. For patients with severe asthma and on oral corticosteroids or with severe asthma and co-morbid moderate-to-severe AD or adults with co-morbid severe CRSwNP- initial dose of 600 mg, followed by 300 mg Q2W. Asthma children (6-11y/o): Body weight 15kg-<30 kg- 300 mg Q4W. Body weight 30kg-<60 kg- 200 mg Q2W; or 300 mg Q4W. Body weight ≥60 kg- 200 mg Q2W. For paediatric patients (6-11y/o) with asthma and co-morbid severe atopic dermatitis, as per approved indication, the recommended dose should follow AD children (6-11y/o). Patients receiving concomitant oral corticosteroids may reduce steroid dose gradually once clinical improvement with dupilumab has occurred. The need for continued dupilumab therapy should be considered at least annually as determined by a physician. CRSwNP: Initial dose of 300 mg, followed by 300 mg Q2W. Consider discontinuing treatment in patients who have shown no response after 24 weeks. PN: Initial dose of 600 mg (two 300 mg injections), followed by 300 mg Q2W. Dupilumab can be used with or without topical corticosteroids. Consider discontinuing treatment in patients who have shown no response after 24 weeks. EoE: 300 mg QW. Dupilumab 300 mg QW has not been studied in patients with EoE weighing <40 kg. Dosing beyond 52 weeks has not been studied. COPD: 300 mg Q2W. Consider discontinuing treatment in patients who have shown no response after 52 weeks. For Missed dose instructions, please refer to the full prescribing information. **Contraindications:** Hypersensitivity to dupilumab or any of the excipients. **Precautions:** Not be used to treat acute symptoms, acute exacerbations of asthma or COPD, acute bronchospasm or status asthmaticus. Do not discontinue corticosteroids abruptly upon start of dupilumab. Reduction should be gradual and performed under supervision of a physician; it may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy. Biomarkers of type 2 inflammation may be suppressed by systemic corticosteroid use. If systemic hypersensitivity reaction occurs, discontinue dupilumab and initiate appropriate therapy. Be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in patients with eosinophilia. Treat pre-existing helminth infections before initiating dupilumab. If patients become infected while receiving dupilumab and do not respond to anti-helminth treatment, discontinue dupilumab until infection resolves. Cases of enterobiasis were reported in children 6 to 11 years old in the paediatric asthma development program. Advise patients to promptly report new onset or worsening eye symptoms. Patients who develop conjunctivitis, dry eye and keratitis that does not resolve following standard treatment should undergo ophthalmological examination. Sudden changes in vision or significant eye pain that does not settle warrant urgent review. Patients with comorbid asthma should not adjust or stop asthma treatments without consultation with physicians. Carefully monitor patients after discontinuation of dupilumab. Avoid using live and live attenuated vaccines concurrently with dupilumab. Patients should be brought up to date with immunisations before starting dupilumab. **Drug Interactions:** Immune responses to TdaP vaccine and meningococcal polysaccharide vaccine were assessed. Patients receiving dupilumab may receive concurrent inactivated or non-live vaccinations. **Pregnancy and lactation:** Should be used during pregnancy only if potential benefit justifies potential risk to foetus. Unknown whether dupilumab is excreted in human milk or absorbed systemically after ingestion. Decision must be made whether to discontinue breast-feeding or dupilumab taking into account benefit of breast feeding for the child and benefit of therapy for the woman. **Undesirable effects:** Most common adverse reactions reported- injection site reactions, conjunctivitis, conjunctivitis allergic, arthralgia, oral herpes, eosinophilia and injection site bruising. Safety profile observed in adolescents and children 6 months to 11 years old consistent with that seen in adults. For other undesirable effects, please refer to the full prescribing information. **Preparation:** 2 x 300mg/2ml in pre-filled syringe with needle shield, 2 x 200mg/1.14ml in pre-filled syringe with needle shield. **Legal Classification:** Part 1, First & Third Schedules Poison **Full prescribing information is available upon request.**

MAT-HK-2400891-1.0-12/2024

API-HK-DUP-24.12

sanofi

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http://www.sanofi.hk/
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DUPIXENT® (dupilumab)

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 prior 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)