

ACADEMIC PUBLICATION SET

VIEN GUT MODEL

Integrated Outpatient Care for Complex Chronic Multimorbidity

Part C — Verification targets on target organs

Vien Gut Model Academic Publication Set

DOCUMENT C.1

MULTI-CENTER VERIFICATION INVITATION

VERIFICATION TARGET: CRYSTAL-FREE AT TIME OF ASSESSMENT

Vien Gut Model — Academic Publication Set

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C.1 — Crystal-Free at time of assessment

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INTRODUCTION

In 2007, Viện Gút comprised two affiliated units: the Viện Gút Polyclinic and the French-Vietnamese Center for Gout and Chronic Disease Research (formerly the Gout Research Institute), which simultaneously provided treatment and conducted research to find solutions for patients with severe complicated gout accompanied by complex chronic multimorbidity. During this journey, in 2014 we established a research collaboration with Professor Thomas Bardin of Université Paris 7, France, co-author of the EULAR gout treatment recommendations from 2006 to the present [1, 3]. Notably, EULAR 2006 was the first international guideline in the world to affirm the principle that gout can be cured. Through Professor Thomas Bardin, Viện Gút expanded its research collaboration with Professor Pascal Richette, co-author of EULAR recommendations from 2016 to the present, and Professor Nicola Dalbeth, co-author of the ACR 2012 and 2020 gout treatment recommendations [2, 5]. Professor Thomas Bardin personally guided Viện Gút in applying the treat-to-target strategy for patients at Viện Gút from 2014. The treatment results of urate crystal dissolution for severe gout using the treat-to-target (T2T) strategy were published at ACR 2017, ACR 2020, EULAR 2019, and several other prestigious international medical journals [18].

In 2018, when Viện Gút undertook to apply the treat-to-target strategy for patients with severe complicated gout accompanied by complex chronic multimorbidity, Professor Thomas Bardin connected with numerous professors and physicians from France — world-leading experts in cardiology, nephrology, hepatology, diabetology, diagnostic imaging, molecular biology, cell biology, immunology and biostatistics — to collaborate in research with Viện Gút. However, gout treatment and comorbidity guidelines had only developed the WHAT component well. To apply the treat-to-target strategy safely and effectively for patients with severe complicated gout accompanied by complex chronic multimorbidity, from 2018 onward Viện Gút focused on researching and developing HOW and DATA-to-operate. Based on the HOW and DATA-to-operate foundation, from 2019 Viện Gút identified windows of opportunity for some gout patients with end-stage chronic kidney disease to conserve renal function for many years, reduced decompensation in some patients with heart failure with reduced ejection fraction, and achieved recompensation in some patients with end-stage liver cirrhosis. In 2024, Viện Gút began verifying the crystal-free target for gout patients. From July 2024 to January 2026, 155 gout patients in the guideline-covered and borderline zones achieved crystal-free status.

Document C.1 comprises 6 Parts. Part 1 — Receiving WHAT from gout treatment and comorbidity guidelines. Part 2 — Gaps in gout treatment and comorbidity guidelines. Part 3 — Integrating WHAT from gout treatment and comorbidity guidelines with HOW and DATA-to-operate. Part 4 — Which guideline gaps the Vien Gut Model addresses. Part 5 — How physicians and the multidisciplinary team operate WHAT + HOW + DATA-to-operate for gout and comorbidity treatment. Part 6 — Crystal-free target verification results.

PART 1 — Receiving WHAT from gout treatment and comorbidity guidelines

1. The principle that gout can be cured

In 2014, through Professor Thomas Bardin — co-author of the EULAR 2006 Recommendations — Viện Gút received the most fundamental principle in gout treatment. Recommendation No. 8 of EULAR 2006 [1] states: *“Gout is a true crystal deposition disease that occurs only when monosodium urate crystals are present. If the process of urate crystal formation continues to be prevented in the patient and existing crystals are dissolved, the patient is essentially ‘cured’.”*

The principle that gout can be cured, consistently reaffirmed by ACR 2020 [5] and 16 international guidelines and their updated versions over nearly two decades, has further strengthened Viện Gút’s conviction that the goal of curing gout is achievable in clinical practice.

2. Receiving the treat-to-target strategy

Professor Thomas Bardin personally guided Viện Gút in applying the treat-to-target (T2T) strategy from 2014: gradually titrating urate-lowering therapy (ULT — allopurinol or febuxostat) until serum uric acid (sUA) reached the target below 360 $\mu\text{mol/L}$ (6 mg/dL) per EULAR/ACR [1, 3, 5], or below 300 $\mu\text{mol/L}$ (5 mg/dL) for gout with active tophi to promote dissolution of deposited urate crystals and prevent new crystal formation.

The treatment results of urate crystal dissolution for severe gout using the T2T strategy at Viện Gút were published at ACR 2017, ACR 2020, EULAR 2019, and several other prestigious international medical journals [18].

Beyond receiving the treat-to-target strategy from gout treatment guidelines, Viện Gút also collaborated with Professor Thomas Bardin and colleagues in France and the University of Medicine and Pharmacy of Ho Chi Minh City to research the association between HLA-B*5801 and skin reactions to allopurinol in Kinh people in Ho Chi Minh City. This research — published on ScienceDirect (2019) [15, 16, 17] — contributed to establishing the HLA-B*5801 screening protocol before initiating allopurinol, ensuring patient safety during the ULT titration phase.

3. Receiving guidance on acute gout flare management

Guidelines clearly state: during the ULT titration phase, patients are at risk of acute gout flares due to the crystal dissolution process releasing MSU into the joint fluid. EULAR and ACR recommend flare prophylaxis [1, 3, 5] with low-dose colchicine, NSAIDs, or short-course corticosteroids throughout the titration phase. Gradual tapering and cessation of prophylaxis after 3–6 months once sUA has reached a stable target and flares have ceased. However, the recurrence of acute gouty arthritis due to the urate crystal dissolution process in many patients is extremely complex and is the primary reason patients discontinue urate-lowering therapy. This is precisely the challenge that the Vien Gut Model has focused on resolving over nearly two decades.

4. Benchmarking joint ultrasound for urate crystal monitoring against international guidance

4.1. Viện Gút has studied joint ultrasound since 2012

Viện Gút began deploying joint ultrasound for gout patients in 2012, at a time when virtually no reference material existed on ultrasound identification of urate crystal deposits in joints and tendons. The vast majority of patients had severe complicated gout — many had carried the disease for 10–20 years without proper urate-lowering treatment, presenting with dozens of tophi of varying sizes and severe deformities.

To overcome the lack of reference materials, Viện Gút adopted a gross pathology–ultrasound correlation method: during tophus surgery, physicians directly observed the layer of urate crystals forming a white membrane on the underlying cartilage surface — the very structure producing the double contour sign on ultrasound. Through this direct visual correlation method, Viện Gút ultrasound physicians were able to distinguish true double contour from pseudo double contour cases. Additionally, ultrasound detected tophi that clinical examination could not identify with the naked eye — the actual tophus burden was far greater than clinical assessment suggested.

4.2. 2015: OMERACT confirmation

The OMERACT Ultrasound Gout Task Force (Gutierrez et al.) [7] published an international consensus on four standard ultrasound lesions in gout: double contour sign, tophus, aggregates, and erosion. Viện Gút observed that its ultrasound research deployed since 2012 — particularly the gross pathology–ultrasound correlation method for identifying double contour and tophi — was consistent with the definition system that OMERACT published three years later. This reinforced the conviction that the direction Viện Gút had chosen was correct from the outset.

4.3. 2014: comparing ultrasound and DECT — choosing ultrasound

Viện Gút collaborated with the Medic Medical Center (Ho Chi Minh City) to compare joint ultrasound with DECT (Dual-Energy CT). Results: ultrasound detected double contour that DECT could not distinguish; ultrasound was radiation-free, infinitely repeatable, low-cost, provided results in the outpatient setting, and was deployable in LMICs. DECT had the advantage of whole-body crystal volume quantification but involved ionizing radiation, very high cost, and scarce equipment in LMICs. Viện Gút decided to choose ultrasound as the primary imaging method, not DECT.

4.4. Choosing caliper mm² — not the semi-quantitative scale

Since 2012, Viện Gút chose to measure tophus size using caliper on ultrasound (mm² = length × width) rather than qualitative classification. Three reasons: (1) Full disease spectrum coverage — measuring from the smallest tophi (~5 mm²) to the largest (~2,000 mm²), whereas qualitative scales cannot distinguish actual size; (2) Compatible with standard practice — caliper measurement is the most basic skill that all ultrasound physicians worldwide perform daily, requiring no additional training; (3) Reflects changes at 3-month intervals — tophi from 50×30 mm down to 40×25 mm, patients see progress on screen, maintaining treatment motivation.

In 2021, when OMERACT developed the 0–3 semi-quantitative scale [8], Viện Gút conducted an internal study comparing the two methods: caliper mm² was easier to perform as it aligned with standard daily practice; the 0–3 scale required subjective estimation by physicians, with greater inter-observer variability. Viện Gút continues to operate with caliper mm² and places the OMERACT 0–3 method alongside for benchmarking — not as a critique, but presenting the two systems in parallel.

5. Receiving WHAT from comorbidity guidelines

When expanding treatment for patients with severe complicated gout accompanied by multimorbidity, Viện Gút simultaneously received WHAT from comorbidity guidelines: KDIGO [9] for chronic kidney disease (CKD staging, eGFR thresholds for medication adjustment), ESC [10] for heart failure (NYHA classification, fluid management, baseline medications), EASL [11] for liver cirrhosis (Child-Pugh classification, ascites management), ADA [12] for diabetes (HbA1c targets, insulin management when using corticosteroids).

Viện Gút recognized: **gout guidelines and comorbidity guidelines are written separately, without integration with each other.** The gout guideline does not mention how to titrate ULT when eGFR is below 30. The kidney guideline does not mention gout. The cardiac guideline does not reference liver disease. Each guideline is complete within its own axis but creates an “overlapping blind zone” (double blind zone) where axes intersect — where physicians have no guidance to apply.

Part 1 Conclusion: Viện Gút fully received WHAT: the principle that gout can be cured (18 guidelines [1–6]), the T2T strategy, flare management, OMERACT ultrasound (benchmarked and developed caliper mm² since 2012), and comorbidity guidelines. However, WHAT only answers “what to do” — it does not answer “how to do it” when patients have complex multimorbidity. Part 2 will identify these gaps specifically.

PART 2 — Gaps in gout treatment and comorbidity guidelines

1. Guideline viết cho ai

Gout treatment and comorbidity guidelines are written for the general medical community — without distinguishing between outpatient or inpatient settings, LMIC or HIC, single disease or multimorbidity. When

patients have uncomplicated gout, physicians can apply guidelines directly without significant difficulty. But when patients have severe complicated gout with CKD G4–G5, heart failure NYHA III–IV, decompensated cirrhosis — physicians face the patient with no specific guidance to apply.

2. Patient zoning by level of guideline coverage

To analyze gaps systematically, Viện Gút classified gout patients into three zones — not by disease severity but by the extent to which guidelines can guide clinical action for that specific case.

2.1. Guideline-covered zone: Uncomplicated gout or gout with 1–2 mild, well-controlled comorbidities.

- **What physicians can do:** Direct guideline application. Standard-dose allopurinol or febuxostat titration. Flare prophylaxis with colchicine or NSAIDs. sUA monitoring per T2T strategy. Basic HOW is sufficient.
- **What physicians cannot yet do:** Crystal-free confirmation — no guideline standardizes a method for confirming complete crystal dissolution. Monitoring crystal dissolution by ultrasound — lack of interdisciplinary coordination between rheumatologists and ultrasound physicians. Knowing when the patient has truly achieved crystal dissolution even though sUA has reached target.

2.2. Borderline zone: Gout with 2–3 comorbidities with treatment conflicts (e.g., CKD stage 3, mild-to-moderate heart failure).

- **What physicians can do:** Knows WHAT to do from guidelines (lower sUA, flare prophylaxis). Basic prescribing when no serious conflicts exist.
- **What physicians cannot yet do:** ULT titration when renal function is declining (fluctuating eGFR, DRESS/SJS risk) — no protocol exists. Resolving conflicts when 1–2 flare medication classes are contraindicated by comorbidities — guidelines do not guide substitute selection. Integrated risk stratification — each guideline stratifies its own axis alone, none integrates into a comprehensive picture.

2.3. Beyond-guideline zone: Severe complicated gout with CKD G4–G5, decompensated cirrhosis Child-Pugh B/C, heart failure NYHA III–IV.

- **What physicians can do:** Virtually no guidance from any guideline. Patients are excluded from most RCTs — evidence does not exist for this group.
- **What physicians cannot yet do:** Safe ULT titration when both allopurinol and febuxostat are severely limited. Flare control when all three medication classes (colchicine, NSAIDs, corticosteroids) are contraindicated or severely limited. Deciding whether to continue or pause ULT when multi-organ decompensation occurs — no guideline provides guidance. All treatment decisions fall within the blind zone.

The three zones lie on a continuous spectrum — patients can move between zones as disease progresses. Patients are zoned by their most severe criterion: for example, mild gout + CKD G5 → beyond-guideline zone.

Zoning conclusion: The three zones reveal a clear gradient: from the guideline-covered zone (guideline provides sufficient WHAT, lacking crystal-free confirmation) through the borderline zone (WHAT begins to weaken, HOW is empty) to the beyond-guideline zone (guidelines are silent, physicians have no tools). This gradient is not because guidelines are poorly written — but because guidelines are designed for single diseases, while clinical reality is multimorbidity. The more complex, the more isolated the physician before the patient.

3. Cumulative gaps across three zones

3.1. Guideline-covered zone — 4 initial gaps

- (1) Lack of interdisciplinary coordination with OMERACT ultrasound [7] — rheumatologists prescribe medications but do not coordinate with ultrasound physicians to monitor the crystal dissolution process.

- (2) The RCT evidence pyramid has not proven crystal-free — the NOR-Gout study only demonstrated remission.
- (3) No guideline standardizes a method for confirming crystal-free as a measurable endpoint.
- (4) Historical gap — before 2015 there was no OMERACT [7] standardization of gout ultrasound signs.

3.2. Borderline zone — 5 cumulative gaps

The four gaps from the guideline-covered zone do not disappear but accumulate and are amplified:

- (1) Medication conflicts without protocol — when 1–2 gout medications are limited by comorbidities, guidelines do not guide substitute selection.
- (2) ULT titration when renal function is declining — fluctuating eGFR, increased DRESS/SJS risk.
- (3) Integrated risk stratification does not exist — each guideline stratifies separately, none integrates.
- (4) OMERACT ultrasound [7, 8] is more difficult when patients have multiple tophi and multi-joint involvement.
- (5) Minimum multidisciplinary team composition is not guided.

3.3. Beyond-guideline zone — 6 systemic gaps

All gaps accumulate to the maximum level, and additional ones emerge:

- (1) All medications are limited — allopurinol, febuxostat, colchicine, NSAIDs, corticosteroids alike.
- (2) Titration on a multi-organ damage background — each ULT dose increase requires simultaneous assessment of kidney, heart, liver.
- (3) Double blind zone — when patients experience cardiac/renal/hepatic decompensation during ULT titration, no guideline guides whether to continue or pause.
- (4) The Clinical Conductor does not exist in the current healthcare system.
- (5) DATA-to-operate does not exist — no healthcare facility has a multi-axis longitudinal monitoring system.
- (6) A complete multidisciplinary team is not organized.

Part 2 Conclusion: HOW gaps accumulate along a gradient: 4 gaps in the guideline-covered zone, 5 in the borderline zone, 6 in the beyond-guideline zone. These are not gaps of a single guideline or a single specialty — these are structural gaps of the entire healthcare system in its approach to complex chronic multimorbidity. WHAT exists but HOW is empty — and the more complex, the emptier.

PART 3 — Integrating WHAT from gout treatment and comorbidity guidelines with HOW and DATA-to-operate

1. Three-layer framework WHAT + HOW + DATA-to-operate

The Vien Gut Model operates on a three-layer framework: WHAT (guideline knowledge), HOW (operational organization), and DATA-to-operate (continuous measurement and monitoring). The three layers are inseparable — they operate simultaneously, continuously, for each patient, at every follow-up visit. WHAT indicates what needs to be done. HOW indicates how to do it in the multimorbidity context. DATA-to-operate indicates where the patient stands on the journey and what adjustment is needed next.

The complete HOW and DATA-to-operate of the Vien Gut Model are presented in detail in Part B — Operational Model, comprising 5 documents. Each document covers a specific operational layer in the gout and comorbidity treatment journey:

- **B.1. First visit examination** — Activating the integrated operational system: channeling to the Clinical Conductor, multidisciplinary team and safety valve for referral.

- **B.2. Outpatient treatment plan** — WHAT–HOW–DATA-to-operate architecture across 4 treatment phases: from managing the complex phase to sustainable maintenance.
- **B.3. Necessary and sufficient conditions for finding the window of opportunity** — Integrating safety valves, polypharmacy management, adherence capacity, disease status — from guideline limitations to the body's recovery capacity.
- **B.4. Patient role** — Operational framework from the patient and family perspective: from passive recipients to measurable participation capacity, training and longitudinal follow-up management.
- **B.5. Enabling conditions and priority principles** — When complex chronic multimorbidity coexists in a single patient: controlling comorbidities is not to achieve independent targets but to keep the window of opportunity open.

Part 3 below summarizes how Viện Gút integrates guideline WHAT into each step of the operational process described in B.1–B.5.

2. Integrating WHAT from gout treatment and comorbidity guidelines into the Vien Gut Model HOW

2.1. In examination and diagnosis

WHAT guidelines require: MSU crystal confirmation (gold standard for gout diagnosis). Baseline sUA assessment. Comorbidity assessment: CKD staging (eGFR), heart failure classification (NYHA, EF), cirrhosis grading (Child-Pugh), HbA1c.

HOW của Viện Gút: Incorporating all above requirements into the mandatory first-visit protocol. Adding baseline caliper mm² ultrasound (target tophus). Baseline X-ray. T1–T4 stratification at the first visit. Determining patient zone (guideline-covered / borderline / beyond-guideline). Detailed reference: B.1.

2.2. In outpatient treatment planning

WHAT guidelines require: T2T strategy: ULT selection (allopurinol or febuxostat), sUA target below 360 µmol/L or below 300 µmol/L when tophi are present. Flare prophylaxis during the titration phase. Lifelong ULT maintenance.

HOW của Viện Gút: Treatment planning across 4 phases (Acute stabilization → Titration → Maintenance → Crystal-free assessment). Defining follow-up SLA by phase and stratification. Designing individualized pathways for each patient based on T1–T4 stratification. Detailed reference: B.1, B.2.

2.3. In ULT titration

WHAT guidelines require: Gradual ULT dose escalation until sUA target is reached. EULAR/ACR recommend low starting dose, increasing every 2–4 weeks.

HOW của Viện Gút: Multi-axis protocol — each dose increase requires simultaneous assessment of eGFR, liver function, cardiovascular status before deciding. HLA-B*5801 screening [15, 20] before initiating allopurinol. Monitoring drug allergy risk (DRESS/SJS) during the first 3 months. Febuxostat prioritized when CKD G4–G5. Pause/dose-reduction thresholds when another disease axis deteriorates. Detailed reference: B.2.

2.4. In acute gout flare management

WHAT guidelines require: Low-dose colchicine, NSAIDs, or short-course corticosteroids for flare prophylaxis and acute flare treatment.

HOW của Viện Gút: Stratifying flare severity. Identifying which medications can still be used at minimum safe doses when 1–3 medication classes are limited by comorbidities. Combining multi-target natural anti-

inflammatory compounds (NF-κB, NLRP3) as supportive foundation. Adjusting enabling conditions (blood glucose, blood pressure, electrolytes) to reduce the systemic inflammation threshold. Detailed reference: B.2.

2.5. In patient guidance

WHAT guidelines require: Patient education on the nature of gout (chronic disease, not just joint pain episodes). Dietary and lifestyle guidance. Explaining the importance of lifelong ULT adherence. ACR 2020 [5] strongly recommends shared treatment decision-making with patients.

HOW của Viện Gút: Visual medicine — the most effective patient guidance tool: every 3 months patients see on ultrasound that tophi are shrinking, that crystals are dissolving — maintaining treatment motivation. Standardized before–after clinical photographs so patients see progress with their own eyes. Explaining why lifelong ULT maintenance is needed after achieving crystal-free: crystal-free at the time of assessment, not permanently cured — stopping ULT carries a risk of crystal re-deposition. Guiding patients to recognize signs requiring early follow-up. Building a long-term collaborative relationship between physician and patient — the foundation for multi-year longitudinal follow-up. Detailed reference: B.3, B.4.

2.6. In longitudinal follow-up and crystal-free assessment

WHAT guidelines require: Regular sUA monitoring. EULAR 2023 [6] recommends ultrasound for diagnosis and monitoring.

HOW của Viện Gút: Caliper mm² ultrasound every 3 months (target tophus). X-ray every 12 months. Standardized clinical photographs at each follow-up. T1–T4 stratification updated at each follow-up. Crystal-free = caliper mm² = 0 at all previously recorded sites, confirmed at least 2 times 6 months apart. Detailed reference: B.2, B.3.

2.7. In polypharmacy management and conflict resolution

WHAT guidelines require: Each guideline prescribes medications for its own disease axis. No guideline integrates.

HOW của Viện Gút: The Clinical Conductor manages the entire medication interaction matrix — not just gout–comorbidity drug pairs but all medications in use. Priority principle when conflicts arise: vital organs first (Heart → Kidney → Liver → ULT pace). DATA-to-operate monitors closely after each intervention. Detailed reference: B.4.

2.8. In referral

WHAT guidelines require: Silent — no guideline provides referral guidance for outpatient multimorbidity patients.

HOW của Viện Gút: Safety valve for referral: activation threshold for referring patients to higher-level care when complications exceed outpatient capacity. Standard protocol: who decides, where to refer, what information accompanies the patient, who receives the patient back after stabilization to continue the crystal-free journey. Detailed reference: B.4.

3. DATA-to-operate — continuous monitoring across all above steps

DATA-to-operate is not an electronic medical record (EMR). **EMR stores — DATA-to-operate operates.** This system transforms measurement data into real-time clinical decisions, across three combined measurement layers.

Biochemistry and hematology layer: sUA, eGFR, liver function (albumin, GGT, FibroScan), NT-proBNP, HbA1c, cortisol/ACTH, electrolytes (K⁺). Each parameter has its own action threshold according to T1–T4 stratification.

Imaging layer: OMERACT [7] caliper mm² ultrasound (primary layer), joint X-ray (supplementary layer), standardized clinical photographs (cross-reference layer). The three imaging layers were presented in detail in Part 1, Section 4.

Time series: Crystal-free is not a snapshot at a single point in time — it is the destination of a journey. DATA-to-operate tracks the entire journey: sUA from baseline to target, caliper mm² from maximum deposition to 0, flare frequency gradually declining to complete cessation, clinical tophi shrinking to disappearance.

Part 3 Conclusion: Viện Gút does not rewrite WHAT — it integrates guideline WHAT into each step of the operational process: diagnostic examination, treatment planning, ULT titration, flare management, patient guidance, longitudinal follow-up, polypharmacy management, referral. At each step, guidelines provide WHAT and HOW supplements the operational solution for the multimorbidity context. DATA-to-operate continuously monitors across all steps. This is an architecture that no guideline in the world provides.

PART 4 — Which guideline gaps the Vien Gut Model addresses

Part 2 identified cumulative gaps across 3 zones (4 → 5 → 6). Part 3 presented how Viện Gút integrates WHAT into HOW and DATA-to-operate. Part 4 provides specific cross-referencing: which solution addresses which gap.

1. Addressing gaps in the guideline-covered zone (4/4)

- (1) **Lack of interdisciplinary ultrasound** → Viện Gút: multidisciplinary team with gout-specialized ultrasound physician, caliper mm² ultrasound every 3 months coordinated directly with the Clinical Conductor (B.1, B.2).
- (2) **RCT evidence pyramid has not proven crystal-free** → Viện Gút: 155 crystal-free patients (7/2024–1/2026), proposing multi-center verification to supplement the evidence pyramid.
- (3) **No standardized crystal-free confirmation** → Viện Gút: caliper mm² = 0 method, confirmed at least 2 times 6 months apart, combined with sUA below target and no flares for 12 months — developed since 2012.
- (4) **Historical gap before 2015** → Viện Gút: ultrasound research since 2012, gross pathology correlation through tophus surgery, OMERACT 2015 [7] confirmed consistency (Part 1, Section 4).

2. Addressing gaps in the borderline zone (5/5)

- (1) **Medication conflicts without protocol** → Viện Gút: full interaction matrix of all medications in use, vital organ priority principle Heart → Kidney → Liver → ULT pace (B.4, B.5).
- (2) **ULT titration when renal function is declining** → Viện Gút: multi-axis protocol, simultaneous eGFR/liver/cardiac assessment before each dose increase, HLA-B*5801 screening [15, 20], febuxostat prioritized when CKD G4–G5 (B.2).
- (3) **Integrated risk stratification does not exist** → Viện Gút: T1–T4 system, 8 disease axes, approximately 100 parameters, updated at each follow-up (B.1, B.2).
- (4) **OMERACT ultrasound [7, 8] more difficult** → Viện Gút: target tophus strategy (MTP1 → dissolution → new target), digitized anatomical atlas since 2025, reducing scan time to 10–15 minutes (Part 1, Section 4).
- (5) **Multidisciplinary team is not guided** → Viện Gút: sensor–response chain team, continuous coordination protocol, each member assigned a specific disease axis (B.1).

3. Addressing gaps in the beyond-guideline zone (6/6)

- (1) **All medications are limited** → Viện Gút: combination strategy — flare severity stratification, minimum safe-dose medications, multi-target natural anti-inflammatory compounds (NF-κB, NLRP3), enabling conditions adjustment (B.2, B.5).
- (2) **Titration on a multi-organ damage background** → Viện Gút: multi-axis protocol, each ULT dose increase requires simultaneous kidney, heart, liver assessment before deciding (B.2).
- (3) **Double blind zone** → Viện Gút: the Clinical Conductor decides whether to continue/pause ULT based on real-time DATA-to-operate — independent of single-axis guidelines (B.2, B.3).
- (4) **Clinical Conductor does not exist** → Viện Gút: defined and operated the Clinical Conductor role for 18 years — a general internist with continuous CME updates, viewing the full multimorbidity picture, making integrated decisions (B.1).
- (5) **DATA-to-operate does not exist** → Viện Gút: multi-axis longitudinal monitoring system (sUA + eGFR + EF + albumin + caliper mm² simultaneously), automated action thresholds, phase-based follow-up SLA (B.2).
- (6) **Complete multidisciplinary team is not organized** → Viện Gút: sensor–response chain multidisciplinary team operating under a continuous coordination protocol, not discrete case conferences (B.1).

Part 4 Conclusion: The Vien Gut Model addresses 15/15 gaps identified in Part 2 — from the guideline-covered zone (4/4) through the borderline zone (5/5) to the beyond-guideline zone (6/6). Each gap is specifically cross-referenced with a HOW/DATA-to-operate solution and the corresponding Part B document. This is evidence that the Vien Gut Model is not a piecemeal improvement — but a complete operational architecture filling the entire gap gradient.

PART 5 — How physicians and the multidisciplinary team operate WHAT + HOW + DATA-to-operate

1. Clinical Conductor

1.1. Role and rationale

Patients with severe complicated gout accompanied by complex chronic multimorbidity need one person responsible for overall clinical management — not multiple disconnected specialists. In the Vien Gut Model, this role is called the Clinical Conductor: a general internist with continuous medical education (CME) updates, viewing the full multimorbidity picture, making integrated decisions.

This role is mandatory because no guideline in the world guides how to simultaneously coordinate multiple disease axes in a single patient. When the gout guideline requires increasing ULT dose but the kidney guideline warns that eGFR is declining, the cardiac guideline requires fluid restriction but the patient is experiencing hepatic decompensation — someone must see the full picture to decide. This is precisely the structural gap that Part 2 identified in the borderline and beyond-guideline zones.

1.2. Six core functions

(1) **Examination – diagnosis – treatment prescription:** comprehensive assessment of gout and comorbidities; T1–T4 stratification; determining patient zone (guideline-covered / borderline / beyond-guideline); phased treatment planning.

(2) **Target coordination:** setting sUA, eGFR, EF, HbA1c targets for each patient; balancing targets when disease axes conflict.

(3) Guideline conflict resolution: when gout guideline WHAT conflicts with kidney, cardiac or liver guideline WHAT — the Clinical Conductor decides priorities according to the vital organ protection principle: Heart → Kidney → Liver → ULT pace (B.4, B.5).

(4) Polypharmacy management: reviewing the entire medication interaction matrix — not just gout-comorbidity drug pairs but all 8–15 medications in use. Priority principle when conflicts arise: vital organs first (B.4, B.5).

(5) Longitudinal follow-up rhythm decisions: determining follow-up, laboratory, and ultrasound frequency by phase and stratification. Adjusting rhythm when patients change zones or tiers (B.2).

(6) Safety valve for referral activation: when patients exceed outpatient safety thresholds (acute cardiac, renal or hepatic decompensation), the Clinical Conductor activates referral to a higher-level hospital according to pre-prepared scenarios (B.3).

1.3. Leading the window of opportunity strategy

Beyond the six core functions, the Clinical Conductor in the Vien Gut Model is simultaneously responsible for leading the window of opportunity strategy for each patient — especially for patients in the beyond-guideline zone, where no guidance exists. This strategy comprises four steps:

(1) Identifying latent breaking points and thresholds not to be crossed: early detection of thresholds beyond which patients will decompensate irreversibly — for example, eGFR dropping below the dialysis threshold, EF dropping below the compensation threshold, Child-Pugh stage transition.

(2) Designing a phased plan to reduce risk: not attacking comprehensively from the start but dividing into phases: acute stabilization, titration, maintenance, crystal-free assessment — each phase with its own targets and stopping thresholds.

(3) Prioritizing vital organ protection interventions: when multiple disease axes deteriorate simultaneously, the Clinical Conductor decides which organ to protect first according to the Heart → Kidney → Liver principle, accepting temporary postponement of sUA targets to maintain overall safety.

(4) Maintaining treatment long enough to create reversal opportunity: the window of opportunity does not appear immediately — it requires patience to maintain treatment for months or years within the safety zone, waiting for the moment the body recovers sufficiently to intensify treatment. This is something no guideline describes but is daily clinical reality at Viện Gút (B.3).

2. Multidisciplinary team — sensor–response operating chain

2.1. Organizational principles

The multidisciplinary team (MDT) in the Vien Gut Model is not organized as discrete case conferences but as a continuous operating chain with three principles: (1) Clear assignment — each member has specifically defined core functions and minimum duties. (2) Bidirectional consultation — all members can provide feedback to the Clinical Conductor when abnormal signals are detected, without waiting for orders. (3) Shared responsibility for outpatient safety — safety is not solely the physician's responsibility.

With these three principles, the team operates as a sensor–response chain: each member is a dedicated sensor, detecting change signals on their axis and triggering the Clinical Conductor's response. This is the mechanism that enables detection of windows of opportunity and early detection of breaking points — two tasks that no single-axis guideline can accomplish (B.1).

2.2. Diagnostic imaging physician

Core function: transforming diagnostic imaging from a one-time capture tool into a longitudinal structure–function monitoring tool — detecting recovery opportunities and demonstrating progress.

Minimum duties: designing ultrasound monitoring targets (target tophus, caliper mm²); analyzing image series every 3 months to assess crystal dissolution rate; proactive feedback to Clinical Conductor on recovery or deterioration signs; standardizing imaging data for verification and compliance (Part 1, Section 4).

2.3. Laboratory personnel

Core function: transforming laboratory tests from isolated snapshots into a longitudinal monitoring radar — early detection of breaking points before decompensation.

Minimum duties: designing core laboratory panels by phase (sUA, eGFR, EF, albumin, K⁺, cortisol, GGT, ACTH by stratification); alerting when thresholds are crossed (e.g., eGFR declining >15% in 3 months, K⁺ exceeding 5.5 mmol/L); analyzing time-series trends for early detection of gradual decline; ensuring result-delivery SLA for timely Clinical Conductor action (B.2).

2.4. Clinical pharmacist — GPP pharmacy

Core function: serving as the polypharmacy safety checkpoint and transforming medication handover into a behavioral intervention point to maintain adherence within the window of opportunity.

Minimum duties: reviewing interactions and toxicity of all medications before dispensing; standardizing medication instructions in patient-understandable language; integrating nutrition reminders (purine restriction, salt control, dietary guidelines for renal/hepatic failure); recording adherence at each medication pickup (B.4, B.5).

2.5. Nursing / outpatient monitoring staff

Core function: deploying checklists and early red flag detection at the first point of contact.

Minimum duties: collecting vital data (blood pressure, weight, edema, flare frequency, medication adherence); monitoring adherence through standardized questionnaires at each follow-up; early detection of red flags (fever, increasing edema, chest pain, jaundice) and immediate notification to Clinical Conductor; coordinating early follow-up or referral according to pre-prepared scenarios (B.1, B.3).

2.6. Outpatient longitudinal care coordination staff

Core function: closely tracking home treatment plans and early detection of deterioration phases.

Minimum duties: proactive contact with patients between follow-up visits; cross-checking adherence data (correct dose, correct timing, complete days); supporting early detection of deterioration phases (patient discontinuing medication, missing follow-ups, worsening symptoms) and reconnecting with Clinical Conductor (B.1).

2.7. Media / visual medicine staff

Core function: standardizing before–after photos and videos as operational data; supporting visual medicine to increase adherence and build confidence — the decisive factor for keeping the window of opportunity open.

Minimum duties: standardized clinical photography at each follow-up (angle, lighting, scale); building time-series image sequences for each patient; presenting to patients that tophi are shrinking, crystals are dissolving — maintaining treatment motivation throughout the long journey (Part 1, Section 4).

2.8. Integrated planning and trend analysis support (data/ops support)

Core function: aggregating time-series data and supporting Clinical Conductor evidence-based decision-making.

Minimum duties: preparing multi-axis trend dashboards (sUA + eGFR + EF + albumin + caliper mm² simultaneously); alerting breaking points when parameters exceed thresholds; maintaining decision logs and audit trails for each patient; data quality control for multi-center verification (B.2).

3. Operating across three patient zones

3.1. Guideline-covered zone

Guidelines provide sufficient WHAT. The Clinical Conductor coordinates ULT titration per the T2T strategy. The diagnostic imaging physician adds caliper mm² ultrasound to monitor crystal dissolution and confirm crystal-free — something no guideline standardizes. Laboratory personnel monitor sUA regularly. The clinical pharmacist guides medication use and records adherence. Basic HOW is sufficient. Result: crystal-free.

3.2. Borderline zone

Guidelines have WHAT but shift to conditional/weak evidence. The entire team participates. The Clinical Conductor supplements HOW: multi-axis ULT titration (simultaneous eGFR, liver function, cardiovascular assessment before each dose increase), medication conflict resolution by matrix, integrated T1–T4 risk stratification. Laboratory personnel alert on threshold crossings. The clinical pharmacist reviews polypharmacy interactions. Nursing detects red flags. Care coordination staff closely tracks adherence. Result: crystal-free.

3.3. Beyond-guideline zone

Guidelines are silent or exclusionary. The entire team operates at high intensity. The Clinical Conductor leads the window of opportunity strategy: identifying breaking points, designing phased plans, prioritizing vital organ protection, maintaining treatment long enough. Diagnostic imaging physicians and laboratory personnel are the primary sensors for detecting windows of opportunity. Data/ops support staff aggregate trend dashboards. Result: safe T2T treatment, crystal dissolution, tophus reduction — but crystal-free not yet achieved for this group. The crystal-free target for the beyond-guideline zone is being pursued.

4. Treatment safety verification on severe comorbidity stages

Based on the HOW and DATA-to-operate foundation, from 2019 Viên Gút identified windows of opportunity for some gout patients in the beyond-guideline zone:

Conserving end-stage renal function before dialysis — some CKD G4–G5 patients received conservative renal function preservation treatment for many years, delaying or avoiding dialysis. Details in Document C.2.

Reducing decompensation in heart failure with reduced ejection fraction — some patients with reduced EF heart failure experienced significantly reduced decompensation. Details in Document C.3.

End-stage cirrhosis recompensation — some Child-Pugh B/C cirrhosis patients achieved recompensation. Details in Document C.4.

Part 5 Conclusion: The Vien Gut Model operates on two tiers: the Clinical Conductor bears overall clinical responsibility with six core functions and the window of opportunity strategy; the seven-position multidisciplinary team operates as a continuous sensor–response chain. Each position has specifically defined core functions and minimum duties. Team mobilization intensity increases with complexity: from the guideline-covered zone (basic HOW sufficient) through the borderline zone (full team) to the beyond-guideline zone (high intensity, led by the window of opportunity strategy). This is an operational architecture that no single-axis guideline provides — and is the prerequisite for achieving the crystal-free results presented in Part 6.

PART 6 — Crystal-free target verification results

Since 2015, Viện Gút has applied the treat-to-target strategy for over 21,000 gout patients from provinces across the country. Because patients travel from locations over 2,000 km away, Viện Gút focuses on the initial treatment phase — the most difficult phase for patients, especially those with severe complicated gout. Initial phase tasks include: (1) titrating urate-lowering medication to below 300 $\mu\text{mol/L}$ while monitoring drug allergy; (2) resolving acute gouty arthritis flares; (3) safely coordinating gout treatment with comorbidities; (4) longitudinal follow-up through at least two ultrasounds 3 months apart so patients directly see crystals dissolving, maintaining treatment motivation. Once stabilized, patients are transferred to healthcare facilities near their homes; Viện Gút maintains only remote support. This is the main reason why among over 21,000 patients, only a small portion has been followed long enough for crystal-free verification.

From 2017 to 2024, many patients achieved crystal-free status, but we considered it only as treatment success. In July 2024, during Professor Thomas Bardin's visit to Vietnam, some patients asked: "Previously you convinced me that dissolving all urate crystals would be considered cured, why are you not certifying us now?" This question compelled us to find the scientific basis for confirming crystal-free as an official verification target.

The scientific basis lies directly in EULAR 2006 Recommendation No. 8 [1]. This recommendation contains two halves. The first half defines gout as a true crystal deposition disease, occurring only when urate crystals are present — not episodic arthritis, not merely a uric acid disorder. The second half sets two simultaneous conditions for cure: (1) preventing new crystal formation — maintaining sUA below the saturation point with ULT; (2) dissolving existing deposited crystals — eliminating the existing crystal stores in joints, tendons, soft tissues. If only condition 1 is met (lowering sUA but existing crystal stores remain), the disease has not ended. If condition 2 is met without maintaining condition 1, the disease will recur. When both are simultaneously satisfied, EULAR concludes the patient is "essentially cured".

However, Recommendation No. 8 states the cure principle but has not transformed it into operational criteria: it does not specify what to measure with, which imaging to confirm with, how long to follow, or which verification standards to use to declare a patient has achieved crystal-free. The gap between "a correct principle" and "how to confirm it in practice" is where medicine after nearly 20 years remains open — and where Viện Gút has filled the gap through clinical practice. The sections below present how Viện Gút defines, measures and verifies the crystal-free target.

1. Definition of crystal-free at time of assessment

Crystal-free is the state of complete dissolution of MSU crystals from all joints, tendons and soft tissues — confirmed by OMERACT [7] ultrasound (caliper $\text{mm}^2 = 0$) at the time of assessment, at least 2 times 6 months apart, combined with sUA continuously maintained below target and no flares for 12 months.

Crystal-free at time of assessment — not a declaration of permanent cure. To maintain crystal-free, patients must protect their achievement by maintaining lifelong urate-lowering therapy.

Distinguishing crystal-free from remission: Remission is a clinical concept — no flares, sUA at target. Crystal-free is an imaging concept — no crystals remaining. Patients may achieve clinical remission yet ultrasound still shows crystals. Crystal-free is a further and more explicit target than remission.

2. Patient data

From July 2024 to January 2026, Viện Gút confirmed **155 patients** achieved crystal-free status by OMERACT ultrasound (caliper $\text{mm}^2 = 0$). This is an observational result from a complex chronic multimorbidity patient cohort at a single center — including patients in the guideline-covered and borderline zones.

Nearly 1,000 patients are on the journey toward crystal-free in a cohort of 2,000 patients/year. Commitment to a minimum 5–10 year longitudinal follow-up.

3. Research methodology

Study design: retrospective case series. Compliant with STROBE [13] (Strengthening the Reporting of Observational Studies in Epidemiology) and PROCESS 2020 [14] (Preferred Reporting of CasE Series in Surgery and Medicine). Crystal-free criteria: caliper $\text{mm}^2 = 0$ across all joints and tendons with recorded deposition, confirmed at least 2 ultrasound examinations 6 months apart, combined with sUA continuously maintained below target and no flares for 12 months.

4. Evidence limitations

Current data has four main limitations: (1) Single center — not yet verified at other centers; (2) Retrospective — not prospective; (3) No control group — compared with historical cohorts or literature; (4) Post-crystal-free longitudinal follow-up not yet long enough — cannot yet conclude on re-deposition rates. These four limitations are the main reason Viện Gút invites multi-center verification rather than self-publishing.

5. Commitments and next steps

Commitment to a minimum 5–10 year longitudinal follow-up. Target to expand crystal-free to patients in the beyond-guideline zone. Multi-center verification plan starting Q3/2026. ReViGore40 [19] (AP-HP, Hôpital Lariboisière, Paris, Prof. Pascal Richette, NCT06669000) is the first center to join. Université Paris Cité has been a direct research partner since 2017.

6. Document scope limitations

Document C.1 presents only the crystal-free verification target on the gout axis. The three remaining verification targets (end-stage renal function conservation before dialysis, cardiac decompensation reduction, hepatic recompensation) are presented in C.2–C.4. Shared HOW: see B.1–B.5. Theoretical foundation: see A.0–A.5.

CONCLUSION

1. Journey summary

Since 2014, Viện Gút has fully received WHAT from 18 gout treatment and comorbidity guidelines through direct collaboration with Professor Thomas Bardin, Professor Pascal Richette and Professor Nicola Dalbeth. In the process of applying the treat-to-target strategy for over 21,000 gout patients — especially those with severe complicated gout accompanied by complex chronic multimorbidity — Viện Gút discovered cumulative HOW gaps along a gradient across three patient zones. To fill these gaps, from 2018 Viện Gút focused on researching and developing HOW and DATA-to-operate, building a two-tier operational architecture (Clinical Conductor + sensor–response chain multidisciplinary team), and from July 2024 began verifying the crystal-free target as a measurable endpoint of the principle that “gout can be cured”.

2. Contributions of Document C.1

Document C.1 clarifies four points:

First, the HOW gap is a structural gap, not a guideline deficiency. Gout treatment and comorbidity guidelines are written separately, for single diseases, on patients selected in RCTs. When patients have complex multimorbidity, single-axis guidelines overlap and create a gradient of 15 gaps across three zones: 4 in the guideline-covered zone, 5 in the borderline zone, 6 in the beyond-guideline zone. These are not gaps of a single guideline or specialty — these are structural gaps of the entire healthcare system in its approach to complex chronic multimorbidity.

Second, the Vien Gut Model is a complete operational architecture filling the entire gradient. The three-layer WHAT–HOW–DATA-to-operate framework, operated by the Clinical Conductor and the sensor–response chain multidisciplinary team, addresses 15/15 gaps identified in Part 2. The model is not a piecemeal improvement but an integrated architecture, built and operated on over 21,000 patients across nearly two decades.

Third, crystal-free at time of assessment is a more explicit verification target than remission. Crystal-free is measurable by caliper $\text{mm}^2 = 0$ ultrasound, confirmed at least 2 times 6 months apart, combined with SUA maintained below target and no flares for 12 months. This is an imaging target — not a clinical target. Patients may achieve clinical remission yet ultrasound still shows crystals. Crystal-free is a further, more explicit target, consistent with the EULAR 2006 [1] principle: when no crystals remain, the material foundation of the disease no longer exists.

Fourth, the same HOW + DATA-to-operate architecture has opened windows of opportunity on severe comorbidity axes. Some gout patients with end-stage renal failure received conservative renal function preservation for many years with stable health; some chronic heart failure patients experienced reduced decompensation; some decompensated cirrhosis patients achieved recompensation. The number of patients achieving these targets remains modest, but the results were achieved through an architected operational system — not lucky individual cases. Viện Gút will report in detail as verification targets in Documents C.2, C.3, C.4.

3. Limitations of Document C.1

Document C.1 presents the methodology and rationale, not yet detailed data publication. Content not yet presented in C.1 includes:

- Detailed data on 155 crystal-free patients (clinical characteristics, stratification, time to crystal-free, distribution across guideline-covered and borderline zones) will be presented in Appendix 1.
- Viện Gút's research on joint ultrasound methodology (caliper mm^2 , comparison with OMERACT 0–3 scale, inter-observer reproducibility, digitized anatomical atlas) will be presented in Appendix 2.
- The three remaining verification targets (end-stage renal conservation, cardiac decompensation reduction, hepatic recompensation) are presented in C.2–C.4.

4. Position within the publication set

Document C.1 belongs to the Vien Gut Model Academic Publication Set with directly supplementary parts: theoretical foundation (A.0–A.5), detailed HOW (B.1–B.5), verification targets on other target organs (C.2–C.4), and the multi-center crystal-free verification invitation (Part D). The publication set is designed so that the international medical community can independently evaluate each component of the Vien Gut Model.

5. Closing statement

Document C.1 is evidence that the HOW gap between guideline principles and clinical practice on complex multimorbidity patients can be filled — and crystal-free is a feasible verification target when the operational architecture is sufficiently complete. Viện Gút is ready to share the entire model — from theoretical foundation, detailed HOW, operational data to verification methodology — with the international medical community as a non-commercial public good, serving gout patients with complex multimorbidity in low- and middle-income countries.

REFERENCES

Gout treatment guidelines

- [1] Zhang W, Doherty M, Bardin T, et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis.* 2006;65(10):1312–1324.
- [2] Khanna D, Fitzgerald JD, Khanna PP, et al. 2012 American College of Rheumatology Guidelines for Management of Gout. Part 1: Systematic Nonpharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia. *Arthritis Care Res.* 2012;64(10):1431–1446.
- [3] Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis.* 2017;76(1):29–42.
- [4] Richette P, Doherty M, Pascual E, et al. 2018 updated European League Against Rheumatism evidence-based recommendations for the diagnosis of gout. *Ann Rheum Dis.* 2020;79(1):31–38.
- [5] FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for Management of Gout. *Arthritis Care Res.* 2020;72(6):744–760.
- [6] Richette P, Doherty M, Pascual E, et al. 2023 EULAR recommendations for the management of gout: an update. *Ann Rheum Dis.* 2024;83(11):1625–1636.

OMERACT ultrasound

- [7] Gutierrez M, Schmidt WA, Thiele RG, et al. International Consensus for ultrasound lesions in gout: results of Delphi process and web-reliability exercise. *Rheumatology (Oxford).* 2015;54(10):1797–1801.
- [8] Hammer HB, Gudbergson H, Engel B, et al. Development and validation of a semiquantitative OMERACT ultrasound scoring system for gout. *RMD Open.* 2021;7(3):e001923.

Comorbidity guidelines

- [9] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024;105(4S):S117–S314.
- [10] McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42(36):3599–3726.
- [11] European Association for the Study of the Liver (EASL). EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. *J Hepatol.* 2018;69(2):406–460.
- [12] American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes—2024. *Diabetes Care.* 2024;47(Suppl 1):S1–S321.

Reporting standards

- [13] von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Ann Intern Med.* 2007;147(8):573–577.
- [14] Agha RA, Sohrabi C, Mathew G, et al. The PROCESS 2020 Guideline: Updating Consensus Preferred Reporting Of CasE Series in Surgery (PROCESS) Guidelines. *Int J Surg.* 2020;84:231–235.

Viện Gút publications

- [15] Do MD, Mai TP, Le Gia HL, et al. Risk factors for cutaneous reactions to allopurinol in Kinh Vietnamese: results from a case-control study. *Arthritis Res Ther.* 2020;22:182.
- [16] Bardin T, Nguyen QD, Bui TMK, et al. HLA-B*5801 et réactions cutanées à l'allopurinol dans la population Kinh d'Ho Chi Minh Ville (Vietnam). *Rev Rhum.* 2019;86(Suppl 1):A148. [Presented at SFR 2018 Congress].
- [17] Bardin T, et al. FRI0227 Risk factors for skin reactions to allopurinol in the Kinh population of Vietnam. *Ann Rheum Dis.* 2018;77(Suppl 2):655. [Presented at EULAR 2018].

- [18] Nguyễn Đình Quang et al. Treatment results of urate crystal dissolution for severe gout using the treat-to-target strategy at Viện Gút. [Presented at ACR 2017, EULAR 2019, ACR 2020 and international medical journals].

Multi-center verification clinical trial

- [19] Richette P (PI). ReViGore40 — Time Required to Dissolve Urate Deposits. AP-HP, Hôpital Lariboisière, Paris. ClinicalTrials.gov Identifier: NCT06669000.

Supplementary references

- [20] Hung SI, Chung WH, Liou LB, et al. HLA-B*5801 allele as a genetic marker for severe cutaneous adverse reactions caused by allopurinol. *Proc Natl Acad Sci USA*. 2005;102(11):4134–4139.
- [21] Richette P, Bardin T. Gout. *Lancet*. 2010;375(9711):318–328.
- [22] Dalbeth N, Gosling AL, Gaffo A, Abhishek A. Gout. *Lancet*. 2021;397(10287):1843–1855.
- [23] Neogi T, Jansen TLTA, Dalbeth N, et al. 2015 Gout Classification Criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheumatol*. 2015;67(10):2557–2568.
- [24] Perez-Ruiz F, Calabozo M, Pijoan JI, Herrero-Beites AM, Ruibal A. Effect of urate-lowering therapy on the velocity of size reduction of tophi in chronic gout. *Arthritis Rheum*. 2002;47(4):356–360.