MOHSIN HAEMATOLOGY ACADEMY

Journal Club & Critical Appraisal

Critical appraisal · 31 July 2026

Structured summary and critical appraisal of a recent high-impact haematology publication — for trainees and practising clinicians.

HAEMOSTASIS & THROMBOSIS NEJM EVID 2026

All-Retinoic Acid plus Eltrombopag for Refractory/Relapsed Immune Thrombocytopenia

Fu H et al. NEJM Evid 2026;5(8):EVIDoa2500333 — Multicentre Randomised Trial (NCT05438875)

KEY FINDINGS

- 18-month sustained response: 60% (29/48) with ATRA plus eltrombopag vs 35% (17/48) with eltrombopag alone — OR 2.78 (95% CI 1.22–6.37), P=0.014; a 25 percentage point absolute gain, NNT approximately 4
- Complete response 79% vs 58% (95% CI for the difference, 2 to 39 percentage points); median response duration 75 vs 37 weeks, HR for relapse 0.45 (95% CI 0.23–0.86)
- Adverse events were comparable between arms, with no grade 3–4 events and no treatment-related deaths

CLINICAL TAKEAWAY

The most interesting second-line ITP signal in some time, using an inexpensive and familiar agent — but not practice-changing on its own. Before any off-protocol use, note that ATRA is strongly teratogenic, so pregnancy must be excluded and effective contraception maintained throughout treatment; it also carries risks of differentiation syndrome and raised intracranial pressure. Pending BSH review.

CRITICAL APPRAISAL NOTE

Open-label, 96 patients, Chinese centres. The notable weakness is baseline imbalance: WHO grade 2–3 bleeding was present in 21% of the combination arm versus 10% of the monotherapy arm at entry. Because the primary endpoint requires the absence of clinically important bleeding, a more heavily bleeding combination arm faced a harder task, not an easier one — so the observed advantage is arguably conservative. The imbalance still complicates clean attribution of effect to ATRA, and a trial this size cannot exclude chance as a contributor.

1B · Level 1 Evidence — Randomised Controlled Trial

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