Lower incidence of TyG-defined insulin resistance after boosted protease inhibitor-to-dolutegravir switch in people with HIV at high cardiovascular risk: NEAT-022

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HIV DRUG THERAPY GLASGOW 2026

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75%

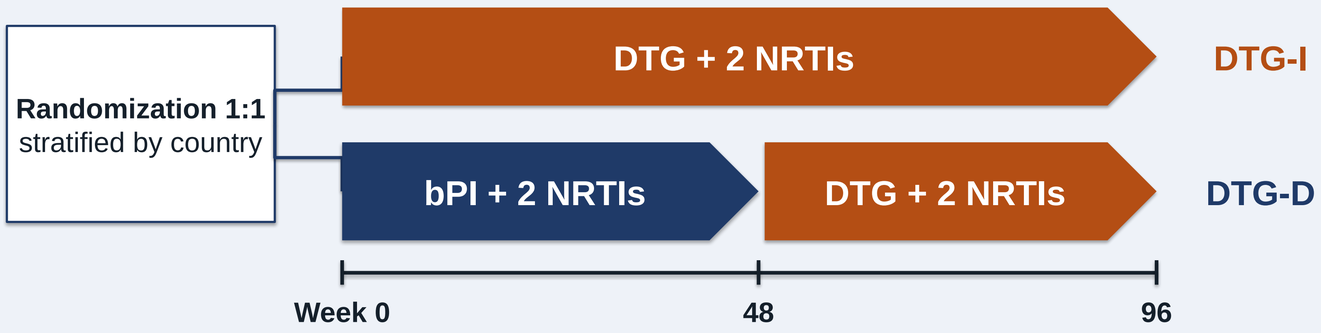
KEY RESULT · PRIMARY ENDPOINT OF THIS POST HOC ANALYSIS

lower incidence rate of TyG-defined insulin resistance with immediate switch to dolutegravir during the randomized phase (weeks 0–48)

20.4 vs **81.7** new cases per 100 person-years · IRR 0.25 (95% CI 0.14–0.45), P<0.0001 · n=178

BACKGROUND & METHODS

Randomized timing of the switch



415 randomized → **412** mITT → prevalence → **178** → incidence (**87** vs **91**)

Insulin resistance (IR) is common in ageing people with HIV (PWH) and rarely measured in switch trials. The **triglyceride–glucose (TyG) index** estimates it from routine fasting labs.

Aim: to test whether switching from boosted protease inhibitors (bPI) to dolutegravir (DTG) lowers TyG-defined insulin resistance.

- Suppressed on 2 NRTIs + bPI; ≥50 years or Framingham >10%; open-label, 32 European sites.

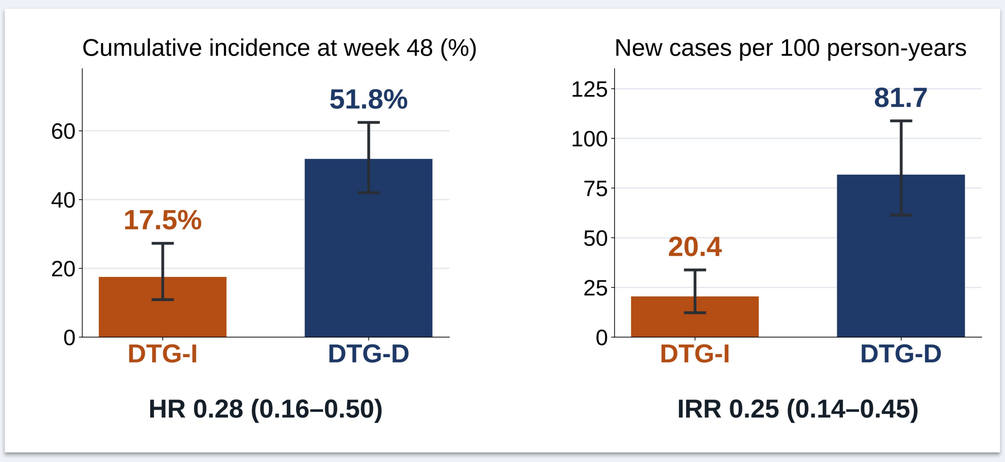
TRIGLYCERIDE–GLUCOSE INDEX

$$TyG = \ln [\ TG \times glucose / 2\ ]$$

fasting values in mg/dL · IR if **TyG ≥ 8.7**

RESULTS · POST HOC PRIMARY ENDPOINT (N=178)

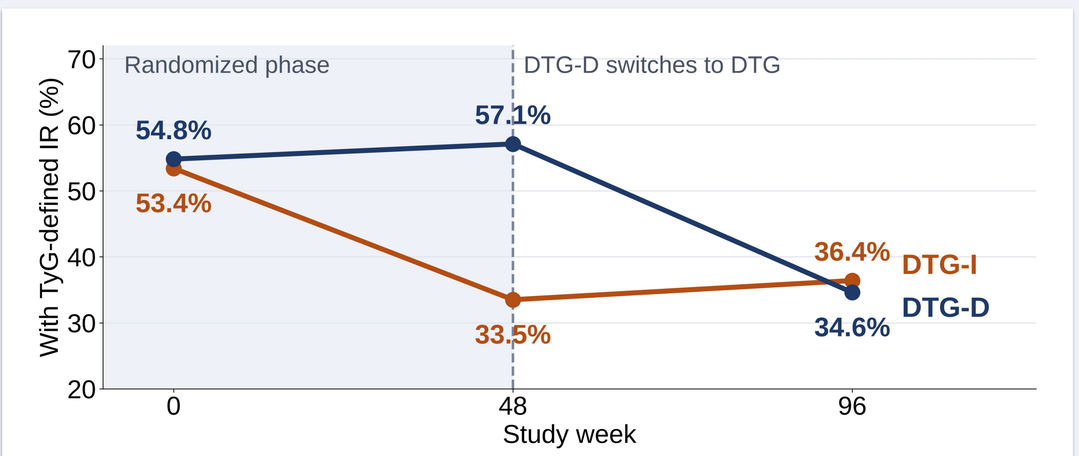
Far fewer new cases after immediate switch



Randomized phase (weeks 0–48), incidence population. Cumulative incidence by Kaplan–Meier with 95% CI; HR from Cox model (log-rank P<0.0001); IRR from Poisson regression (P<0.0001).

RESULTS · TYG-DEFINED IR OVER 96 WEEKS (MITT, N=412)

IR declined after switching in both arms



54.1% (223/412) had TyG-defined IR at baseline. mITT population; dashed line: DTG-D switch at week 48.

RESULTS · SECONDARY ANALYSES

The effect held after adjustment

- **Adjusted model:** immediate switch aIRR 0.25 (0.13–0.45); Framingham >15% aIRR 2.15 (1.22–3.76).
- **Stricter cut-off (TyG >9.1):** IRR 0.33 (0.18–0.63).
- **Weight:** small change (+1.20 vs +0.17 kg at week 48), weakly related to TyG.
- **Weeks 48–96**, both arms on DTG (at risk n=69 vs 43): 13.7 vs 5.3 per 100 PY, descriptive.

Limitations: post hoc; TyG partly reflects triglycerides; mostly male, European population; analyses after week 48 descriptive; clinical outcomes not assessed.

CONCLUSIONS

What this means

Switching from boosted PIs to DTG lowered new TyG-defined IR **early**; the reduction was **not clearly explained by changes in body weight.**

In PWH on bPIs, **routine fasting labs (TyG)** can flag early metabolic risk, and **switching to DTG may improve it.**

NCT02098837 · EudraCT 2013-003704-39 · **Contact:** sempere@clinic.cat · Gatell JM et al. AIDS 2017;31:2503–14; Clin Infect Dis 2019;68:597–606

Abbreviations: aIRR, adjusted incidence rate ratio; bPI, boosted protease inhibitor; DTG, dolutegravir; DTG-I/DTG-D, immediate/deferred switch to DTG; HR, hazard ratio; IR, insulin resistance; IRR, incidence rate ratio; mITT, modified intention-to-treat; NRTI, nucleos(t)ide reverse transcriptase inhibitor; PWH, people with HIV; PY, person-years; TG, triglycerides; TyG, triglyceride–glucose index.

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