RESPOND International Cohort Consortium of Infectious Diseases

Impact of INSTI and TAF-related BMI changes and risk on hypertension and dyslipidemia in RESPOND

Dathan M. Byonanebye, Mark N. Polizzotto, Fernando Maltez, Andri Rauch, Katharina Grabmeier-Pfistershammer, Ferdinand Wit, Stéphane De Wit, Antonella Castagna, Antonella D'Arminio Monforte, Cristina Mussini, Jan-Christian Wasmuth, Eric Fontas, Irene Abela, Mario Sarcletti, Loveleen Bansi-Matharu, Nadine Jaschinski, Sean R Hosein, Vani Vannappagari, Cal Cohen, Emiliano Bissio, Amanda Mocroft, Matthew Law, Lene Ryom, and Kathy Petoumenos, on behalf of the RESPOND study group.

Summary

- **Research Questions**
  - Is current use of INSTI and/or TAF (*versus non-INSTI/TAF regimens*) associated with hypertension (HTN) or dyslipidemia?
  - Is there an interaction between the ART and time-updated BMI?
- **Findings**
  - Current use of INSTIs was associated with incident HTN while TAF was associated with incident dyslipidemia.
  - The association between BMI and HTN or dyslipidemia was not different regardless of ART regimen.
- **Why is it important?**
  - People living with HIV, especially those receiving INSTIs and/or TAF should regularly be screened for hypertension and dyslipidemia.

Introduction

- The use of INSTIs and TAF has been associated with weight gain[1].
- In people with HIV, weight gain is associated with hypertension[2] and dyslipidaemia[3].
- Analyses in selected populations and small cohorts have associated INSTI use and hypertension or dyslipidemia[4-9].
- However, the clinical impact of weight gain associated with INSTIs is not clear.
- We determined whether current use of INSTI and/or TAF (versus regimens without INSTI/TAF) associated with hypertension (HTN) or dyslipidemia?

[1]Bansi-Matharu et al. Lancet HIV, 2021; [2]Brennan et al. EclinicalMedicine, 2022; [3]Galdamez, et al. OFID, 2019; [4]Galdamez, et al. Open Forum Infect Dis 2019; [5]Summers, et al. JAIDS 2020; [6]Brennan, et al. EClinicalMedicine 2022; [7]Saums, et al. Obstetrics and Gynecology 2019; [8]Zash, et al. J Int AIDS Soc 2021; [9]Masenga, et al. Front Cardiovasc Med 2022..

Methods

- HTN was defined as two consecutive BP ≥140/90 mmHg or the initiation of antihypertensives[1].
- Dyslipidemia was defined as total cholesterol >240, or HDL<35, or TRIGs >200 mg/dL, or lipid-lowering therapy[2]
- Multivariable Poisson regression: interaction between time-updated BMI and ART.
- Primary exposures: ART regimens with or without INSTI or TAF.
  - INSTI+TAF, INSTI with no TAF, non-INSTI + TAF, vs no INSTI/TAF (*reference group*).
  - If TDF or EFV was taken prior to current ART, included follow-up after 6 months.
- Adjusted for confounders
  - Demographic, clinical and ART, including exposure to ABC, NVP, IDV, d4T, LPV.
- Baseline date: latest of RESPOND baseline or date of joining local cohort.

[1]Byonanebye et al. HIV Medicine, 2022; [2]Byonanebye et al. AIDS, 2021

Participant eligibility

- Analysis within RESPOND: A consortium of 19 observational HIV cohorts in Europe and Australia
- **Inclusion**
  - Adults (≥18 years)
  - Receiving INSTIs (DTG, BIC, RAL, EVG), or bPIs (DRV, ATV), or NNRTIs (EFV, RPV).
  - Baseline BMI result (within 1 year before baseline) and ≥2 follow-up BMIs
  - ≥2 lipid and blood pressure measures (for the respective analyses)
- **Exclusion**
  - Participants without baseline CD4 and HIV viral load.
  - Participants receiving non-ART medications associated with weight changes[1].

[1]Wharton S et al. Diabetes Metab Syndr Obes 2018

Incidence rate ratios of hypertension

RESPOND International Cohort Consortium of Infectious Diseases

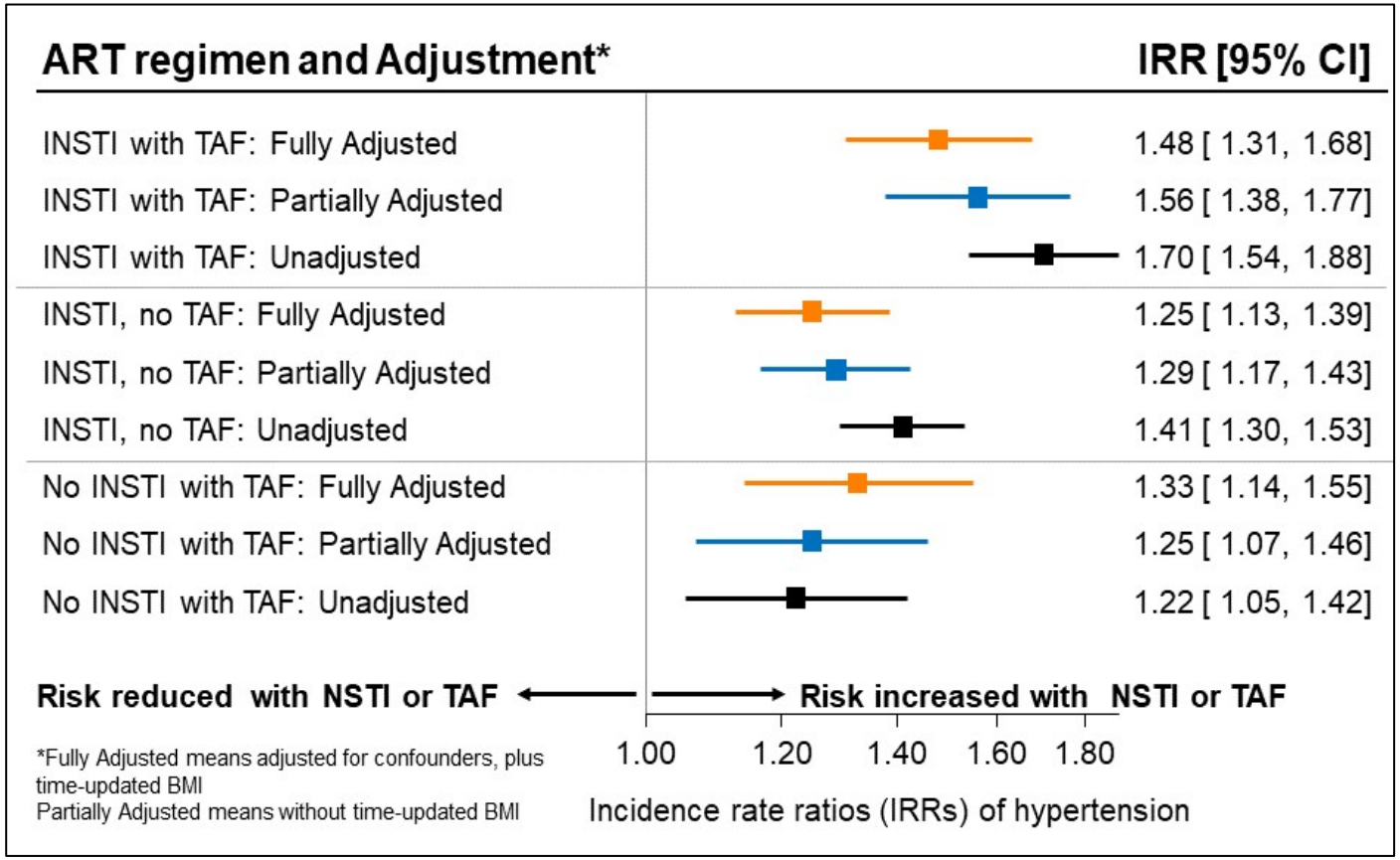
9,704 people followed and 2977 (30.7%) developed hypertension over 39,993 PYFU

Male:76%, White:72% Median age: 44(36–51) years, ART duration: 10 (5–16) years

Current use of INSTI with/out TAF was associated with HTN.

Adjustment for time-updated BMI attenuated the risk.

No interaction between ART and BMI (*interaction p*=0.459).



**Note:* ART and BMI time-updated, ref group=No INSTI or TAF

Incidence rate ratios of dyslipidemia

RESPOND International Cohort Consortium of Infectious Diseases

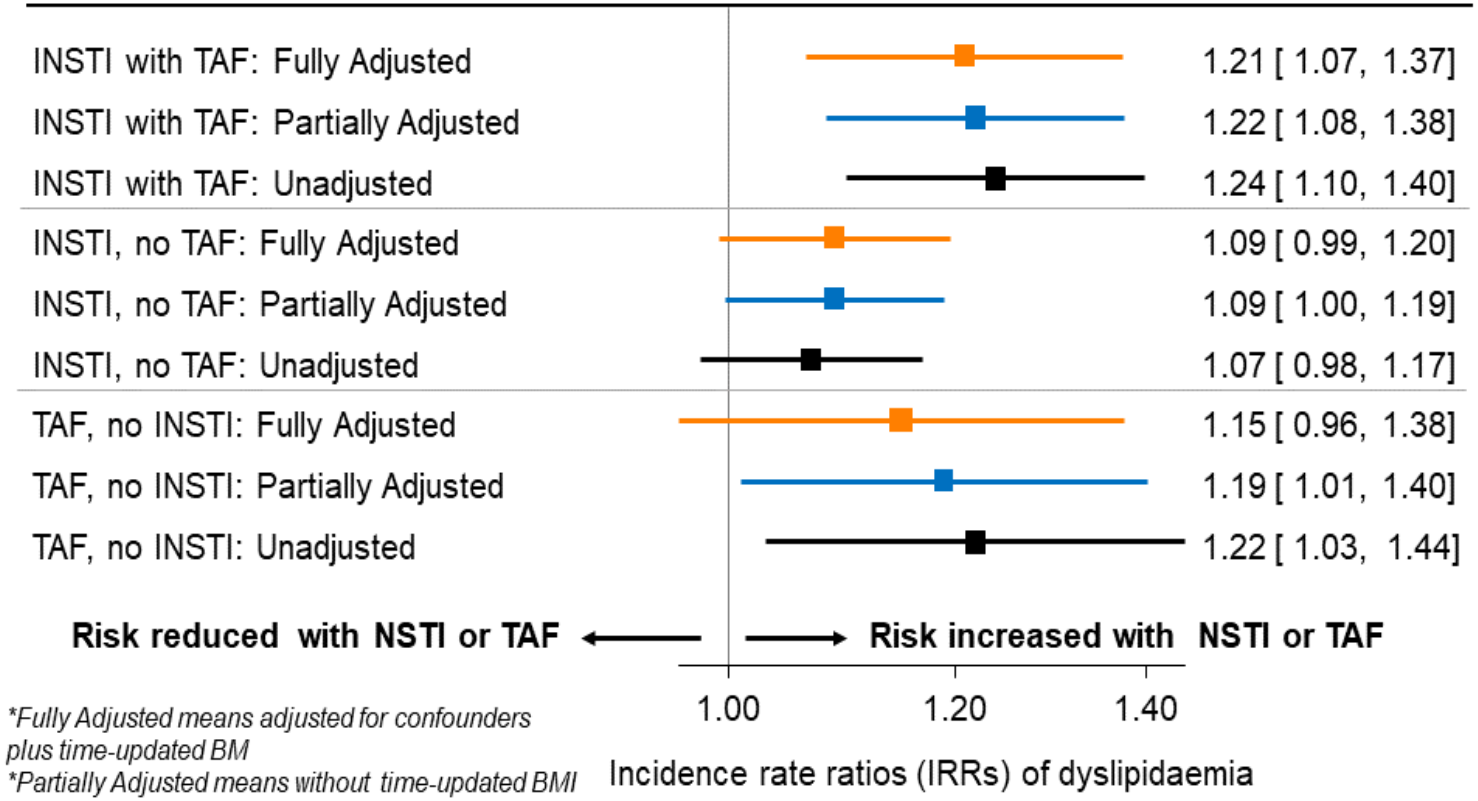
5,231 people followed and 2689 (51.4%) developed dyslipidemia over 19,547 PYFU

Male:73%, White:71% Median age: 43(35–50) years, ART duration: 10 (5–16) years

Current use of TAF with/out INSTI was associated with dyslipidaemia

Adjustment for time-updated BMI attenuated the risk.

No interaction between ART and BMI (*interaction p*=0.303).



**Note:* ART and BMI time-updated, ref group=No INSTI or TAF

Conclusions

- In RESPOND, current use of INSTI was associated with incident hypertension.
- Adjustment for time-updated BMI attenuated the association with hypertension though it remained significant .
- TAF, but not INSTI, was associated with incident dyslipidemia.
- After adjustment for BMI the dyslipidemia association was nonsignificant.
- The relationship between BMI and hypertension or dyslipidemia was not different in people with HIV on INSTI or TAF compared to ART without INSTI or TAF.
- Possible residual confounding: data missing on family history, exercise, and diet.
- Possible intra-class heterogeneity
- However, RESPOND a large, heterogeneous cohort and uses clinic data.

ACKNOWLEDGEMENTS

Cohort principal investigators:
S. De Wit (St. Pierre, Brussels), R. Zangerle (AHICOS), K. Petoumenos (AHOD), F. Wit (ATHENA) G. Wandeler (EuroSIDA), C. Stephan (Frankfurt), N. Chkhartishvili (IDACIRC), C. Pradier (Nice HIV cohort), A. d'Arminio Monforte (ICoNA), C. Mussini (Modena), J. Casabona & J.M. Miro (PISCIS), H. Günthard (SHCS), A. Sönnerborg (Swedish InfCare), C. Smith (Royal Free HIV cohort), J. Begovac (Croatia, HIV cohort), A. Castagna (San Raffaele, Milano), J.C. Wasmuth (Bonn, HIV cohort), J.J. Vehreschild (Cologne, HIV cohort), J. Vera (Brighton HIV cohort).

Cohort coordinator, operational team members and data management:
C. Necsoi, M. Delforge (St. Pierre, Brussels), H. Appoyer, U. Dadogan, G. Leierer (AHIVCOS), J. Hutchinson, D. Byonanebye. (AHOD), M. Van der Valk, M. Hillebregt, T. Rutkens, D. Bergsma (ATHENA), F. Ebeling, M. Bucht, (Frankfurt), O. Chokoshvili, E. Karkashadze (IDACIRC), E. Fontas, K. Dollet, C. Caissotti (NICE, HIV cohort), J. Fanti, A. Tavelli, A. Rodanò (ICoNA), V. Borghi (Modena), A. Bruguera, J. Reyes-Urueña, A. Montoliu (PISCIS), H. Bucher, K. Kusejko, Y. Schaefer (SHCS), L. Mattsson, K. Alenadaf, (Swedish InfCare), F. Lampe, C. Chaloner (Royal Free, HIV cohort), C. Elisabetta, R. Lolatto, A. Lazzarin, A. Poli, S. Nozza (San Raffaele, Milano), K. Mohrmann, J. Rockstroh (Bonn, HIV cohort), M. Scherer, G. Fätkenheuer, N. Schulze, B. Frank, and H. Weiler (Cologne HIV cohort).

RESPOND Scientific Steering Committee:
J Lundgren*, H Günthard*, J Kowalska, D Raben, L Ryom, J Rockstroh, L Peters, O Kirk, D Podlekareva, A Volny Anne, N Dedes, ED Williams, N Chkhartishvili, R Zangerle, K Petoumenos, F Wit, C Necsoi, G Wandeler, C Stephan, C Pradier, A D'Arminio Monforte, C Mussini, A Bruguera, H Bucher, A Sönnerborg, JJ Vehreschild, JC Wasmuth, C Smith, A Castagna, J Vera, J Rooney, I McNicholl, V Vannappagari, H Garges, L Young, R Campo ***Chairs**

Community representatives:
A Volny Anne, N Dedes, L Mendão (European AIDS Treatment Group), E Dixon Williams (UK)

RESPOND Executive Committee:
L Ryom*, M Law*, J Rooney, I McNicholl, V Vannappagari, H Garges, K Petoumenos, G Wandeler, R Zangerle, C Smith, S De Wit, J Lundgren, H Günthard, L Young, R Campo ***Chairs**

RESPOND coordination office, data management and quality assurance:
N. Jaschinski, B. Neesgaard, A. Timiryasova, J.F. Larsen, L. Peters, L. Ryom, O. Fursa, O. Valdenmaiier, M.L. Jacobsen, T. Elsing, S. Shahi, L. Ramesh Kumar, K. Andersen, M. Gardizi, D. Raben

Members of the Scientific Interest Groups:
Hepatitis/Viral Coinfection, Public Health, Outcomes with Antiretroviral Treatment, Tuberculosis, Gender specific outcomes

Statistical Staff:
J. Reekie, L. Greenberg, A. Mocroft, L. Bansi-Matharu, K. Petoumenos, D. Byonanebye, A. Roen, E. Tusch, W. Bannister

Funding:
The International Cohort Consortium of Infectious Disease (RESPOND) has received funding from ViiV Healthcare LLC, Gilead Sciences and Merck Sharp & Dohme. Additional support has been provided by participating cohorts contributing data in-kind and/or statistical support: Austrian HIV Cohort Study (AHIVCOS), The Australian HIV Observational Database (AHOD), CHU Saint-Pierre, University Hospital Cologne, EuroSIDA, Frankfurt HIV Cohort Study, Georgian National AIDS Health Information System (AIDS HIS), Modena HIV Cohort, San Raffaele Scientific Institute, Swiss HIV Cohort Study (SHCS), AIDS Therapy Evaluation in the Netherlands Cohort (ATHENA), Royal Free HIV Cohort Study. AHOD is further supported by grant No. U01-AI069907 from the U.S. National Institutes of Health, and GNT1050874 of the National Health and Medical Research Council, Australia.