

Online Resource 1

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Manuscript title:

Report-level comparator-definition sensitivity in FAERS cardiometabolic disproportionality analysis: A long-acting cabotegravir/rilpivirine HIV pharmacovigilance case study

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The READUS-PV checklist

Section and topic	Item #	Checklist item	Location where item is reported
Title			
	1a	<i>If disproportionality analyses are a prominent component of the published study, the study should be identified as a “disproportionality analysis”. The type of data and name of the database(s) should be specified.</i>	<i>Title</i>
	1b	<i>Report the name of adverse event(s) and/or drug(s) under study, when applicable.</i>	<i>Title</i>
Introduction			
Background	2a	<i>Describe the drug(s) and its utilization, the nature of the adverse event(s) under study and its frequency, and the existing knowledge on the drug-event combination.</i>	<i>Introduction, paragraphs 2–3</i>
	2b	<i>Specify the rationale for performing the analysis, e.g., as part of routine pharmacovigilance, to investigate an overall safety profile, or to assess a pre-specified hypothesis.</i>	<i>Introduction, paragraphs 1–3</i>
	2c	<i>Explain why ICSR databases and disproportionality analysis are suitable to fill the knowledge gap.</i>	<i>Introduction, paragraph 1 and 3</i>
Objectives	3	<i>State specific objectives, identifying the adverse event(s), the drug(s), and the reference</i>	<i>Introduction, paragraph 3</i>

		<i>group, including any pre-specified hypothesis, if applicable.</i>	
Methods			
Study design	4a	<i>Identify the study (i.e., “disproportionality analysis”) and the type of data used (e.g., “individual case safety reports”).</i>	<i>Materials and Methods 4.1</i>
	4b	<i>Provide an outline of the entire study design, including primary and sensitivity analyses performed, and other designs such as case-by-case analysis or literature review.</i>	<i>Materials and Methods 4.1 and 4.4</i>
Data description, access, and pre-processing	5a	<i>Specify the name of the database(s), the database(s) custodian, and the coverage. Specify the type/number of drugs included within the database and the thesaurus, taxonomies, or ontologies used for coding drugs and events.</i>	<i>Materials and Methods 4.1 and 4.3; Supplementary Table S1</i>
	5b	<i>Specify the extraction dates and describe and justify all choices used for data pre-processing, including any data transformation or exclusion, if appropriate.</i>	<i>Materials and Methods 4.1 and 4.2; Figure 1</i>
Variables definition	6a	<i>Describe the study population, including any restriction.</i>	<i>Materials and Methods 4.1 and 4.2; Figure 1</i>
	6b	<i>Describe the nature and the meaning of key variables assessed in the work.</i>	<i>Materials and Methods 4.2 and 4.3</i>
	6c	<i>Specify and justify any grouping of drugs or events. For drugs, specify and justify whether active ingredients/trade names/salts were considered and/or the selected role.</i>	<i>Materials and Methods 4.2 and 4.3; Supplementary Table S1</i>
	6d	<i>Describe any additional data source used, the type of data, and how they interact with ICSRs.</i>	<i>Not applicable; no additional data source was used (Materials and Methods 4.2 and 4.4).</i>

Statistical methods	7a	<i>Present any descriptive analysis performed, specifying variables investigated, statistical tests, and significance thresholds.</i>	<i>Materials and Methods 4.4</i>
	7b	<i>Describe the measure(s) selected for the disproportionality analysis including any threshold used to identify signals of disproportionate reporting. Explain the reason for this choice if applicable.</i>	<i>Materials and Methods 4.4</i>
	7c	<i>Clearly describe any sensitivity analysis and any tool to control confounding, including any restriction, subgroup, stratification, adjustment, or interaction.</i>	<i>Materials and Methods 4.3 and 4.4</i>
	7d	<i>Specify the variables and methods used for the case-by-case analysis, including any algorithm or criteria used to assess causality, if performed.</i>	<i>Not applicable; no case-by-case clinical review or causality adjudication was performed (Materials and Methods 4.4).</i>
	7e	<i>Specify any statistical methods used for other data sources.</i>	<i>Not applicable; no external-data statistical analysis was performed (Materials and Methods 4.4).</i>
Results			
Participants	8a	<i>Specify the number of individual case safety reports included at each stage, including reasons for exclusion.</i>	<i>Results 2.1 and Figure 1; outcome-specific eligible denominators are reported in Figure 2 and Online Resource 2, Tables S7–S9.</i>

	8b	<i>Provide key demographic and clinical characteristics of cases, if possible comparing cases with any appropriate reference group.</i>	<i>Results 2.1; Table 1. Detailed geographic composition is reported in Online Resource 2, Table S5</i>
Disproportionality analysis	9	<i>Present all results including confidence intervals. Present also results of sensitivity analyses, if performed.</i>	<i>Results 2.2–2.5; Figure 2; Tables 2–3; Online Resource 2, Tables S3–S12 and Figures S1–S6</i>
Case-by-case analysis	10	<i>Present the case-by-case analysis of key variables. Present the causality assessment, if applicable.</i>	<i>Not applicable; no case-by-case clinical review or causality adjudication was performed,</i>
Discussion			
Key results	11	<i>Discuss key results with reference to study objectives and contextualize them within the current literature and other consulted sources. Clearly discriminate between expected reactions and emerging safety signals.</i>	<i>Discussion, paragraphs 1–3</i>
External validity	12a	<i>Discuss the external validity of the results to the general population.</i>	<i>Discussion, paragraphs 4–5</i>
	12b	<i>Discuss the potential relevance of results in clinical practice</i>	<i>Discussion, paragraph 5</i>
	12c	<i>Propose further study designs if applicable</i>	<i>Discussion, paragraph 5</i>
Limitations	13	<i>Present general limitations, making clear that disproportionality analysis alone cannot prove causation or measure incidence, and specific limitations, including confounding and reporting bias and efforts to mitigate them.</i>	<i>Discussion, paragraphs 4</i>

Declarations			
	14a	<i>Provide the source of funding/sponsorship and the role of the funders/sponsors for the present study and for any original study on which the present article is based.</i>	<i>Funding</i>
	14b	<i>Clearly identify potential commercial and intellectual conflicts of interest (e.g., link to any drug/event investigated, whether financial, legal action, or software used).</i>	<i>Conflicts of Interest</i>
	14c	<i>Declare any institutional approval needed or granted in the investigation.</i>	<i>Materials and Methods 4.5; Institutional Review Board Statement</i>
	14d	<i>Include a statement on data availability, code availability (including the version of the statistical software used), and protocol registration.</i>	<i>Materials and Methods 4.5; Data Availability Statement</i>

The READUS-PV checklist for abstracts

Section and topic	Item #	Checklist item	Location where item is reported
Background	1a	<i>State the aim/rationale for performing the study.</i>	<i>Background/Objectives paragraph, sentences 1–2</i>
	1b	<i>Specify the adverse event(s) and/or the drug(s) under study, when applicable.</i>	<i>Background/Objectives paragraph, sentence 2; Methods paragraph, sentence 3</i>
	1c	<i>Specify the specific population or setting, when applicable.</i>	<i>Methods paragraph, sentences 1–2</i>
Methods	2a	<i>Identify the study as a “disproportionality analysis” and specify the type of data used.</i>	<i>Methods paragraph, sentence 1</i>
	2b	<i>Specify the name of the database(s) used and the type of access.</i>	<i>Methods paragraph, sentence 1</i>
	2c	<i>Specify the timeframe and geographical region, when applicable.</i>	<i>Methods paragraph, sentence 1</i>

	2d	<i>Specify the disproportionality measure(s) used and their statistical significance threshold(s).</i>	<i>Methods paragraph, sentences 3 and 5</i>
	2e	<i>Specify if a case-by-case analysis is performed.</i>	<i>Methods paragraph, sentence 5</i>
Results	3	<i>Report main findings including their precision (e.g., 95% confidence intervals), together with a short summary of the case-by-case analysis.</i>	<i>Results paragraph, sentences 1–4; case-by-case component not applicable—Methods paragraph, sentence 5</i>
Conclusion	4a	<i>Clearly report key conclusions.</i>	<i>Conclusions paragraph, sentence 1</i>
	4b	<i>Acknowledge that the disproportionality analysis is a hypothesis generating or refinement approach.</i>	<i>Conclusions paragraph, sentence 2</i>
	4c	<i>State the implications and clinical relevance of the findings.</i>	<i>Conclusions paragraph, sentence 1–2</i>