

SUPPLEMENTARY DATA
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SUPPLEMENT 1

This annex includes **tables S1, S2, S3, S4 and S5.**

Table S1. PubMed search strategies

Drugs	Strategies
Integrase inhibitors	Search: integrase strand transfer inhibitor resistance Filters: Meta-Analysis, Systematic Review, from 2000/1/1 - 2023/5/1 Sort by: Most Recent (("integrase inhibitors"[Pharmacological Action] OR "integrase inhibitors"[Supplementary Concept] OR "integrase inhibitors"[All Fields] OR "integrase strand transfer inhibitor"[All Fields] OR "integrase inhibitors"[MeSH Terms] OR ("integrase"[All Fields] AND "inhibitors"[All Fields]) OR ("integrase"[All Fields] AND "strand"[All Fields] AND "transfer"[All Fields] AND "inhibitor"[All Fields])) AND ("resist"[All Fields] OR "resistance"[All Fields] OR "resistances"[All Fields] OR "resistant"[All Fields] OR "resistants"[All Fields] OR "resisted"[All Fields] OR "resistance"[All Fields] OR "resistences"[All Fields] OR "resistent"[All Fields] OR "resistibility"[All Fields] OR "resisting"[All Fields] OR "resistive"[All Fields] OR "resistively"[All Fields] OR "resistivities"[All Fields] OR "resistivity"[All Fields] OR "resists"[All Fields])) AND ((meta-analysis[Filter] OR systematicreview[Filter]) AND (2000/1/1:2023/5/1[pdat]))
Bictegravir	Search: bictegravir resistance Filters: from 2000/1/1 - 2023/5/1 Sort by: Most Recent (("bictegravir"[Supplementary Concept] OR "bictegravir"[All Fields]) AND ("resist"[All Fields] OR "resistance"[All Fields] OR "resistances"[All Fields] OR "resistant"[All Fields] OR "resistants"[All Fields] OR "resisted"[All Fields] OR "resistance"[All Fields] OR "resistences"[All Fields] OR "resistent"[All Fields] OR "resistibility"[All Fields] OR "resisting"[All Fields] OR "resistive"[All Fields] OR "resistively"[All Fields] OR "resistivities"[All Fields] OR "resistivity"[All Fields] OR "resists"[All Fields])) AND (2000/1/1:2023/5/1[pdat]))
Cabotegravir	Search: cabotegravir resistance Filters: from 2000/1/1 - 2023/5/1 Sort by: Most Recent (("cabotegravir"[Supplementary Concept] OR "cabotegravir"[All Fields]) AND ("resist"[All Fields] OR "resistance"[All Fields] OR "resistances"[All Fields] OR "resistant"[All Fields] OR "resistants"[All Fields] OR "resisted"[All Fields] OR "resistance"[All Fields] OR "resistences"[All Fields] OR "resistent"[All Fields] OR "resistibility"[All Fields] OR "resisting"[All Fields] OR "resistive"[All Fields] OR "resistively"[All Fields] OR "resistivities"[All Fields] OR "resistivity"[All Fields] OR "resists"[All Fields])) AND (2000/1/1:2023/5/1[pdat]))
Dolutegravir	Search: dolutegravir resistance prevalence incidence Sort by: Most Recent ("dolutegravir"[Supplementary Concept] OR "dolutegravir"[All Fields] OR "dolutegravir s"[All Fields]) AND ("resist"[All Fields] OR "resistance"[All Fields] OR "resistances"[All Fields] OR "resistant"[All Fields] OR "resistants"[All Fields] OR "resisted"[All Fields] OR "resistance"[All Fields] OR "resistences"[All Fields] OR "resistent"[All Fields] OR "resistibility"[All Fields] OR "resisting"[All Fields] OR "resistive"[All Fields] OR "resistively"[All Fields] OR "resistivities"[All Fields] OR "resistivity"[All Fields] OR "resists"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "incidence"[All Fields] OR "incidence"[MeSH Terms] OR "incidences"[All Fields] OR "incident"[All Fields] OR "incidents"[All Fields])

Table S2. OVID Search Strategies

Drugs	Strategies
Bictegravir	Search Strategy: 1. (bictegravir and incidence and prevalence and resistance).af. (190); 2. limit 1 to full text [Limit not valid in Your Journals@Ovid; records were retained] (68); 3. limit 2 to (clinical trial, phase iii or meta-analysis or observational study or randomized controlled trial or "systematic review") [Limit not valid in BIOSIS Previews, Embase, Journals@Ovid, Your Journals@Ovid; records were retained] (68); 4. limit 3 to dt=20000101-20230531 [January 1st, 2000 to May 31st, 2023] (68); 5. remove duplicates from 4 (34).
Cabotegravir	1. (cabotegravir and incidence and prevalence and resistance).af. (187); 2. limit 1 to full text [Limit not valid in Your Journals@Ovid; records were retained] (58); 3. limit 2 to (clinical trial, phase iii or meta-analysis or observational study or randomized controlled trial or "systematic review") [Limit not valid in BIOSIS Previews, Embase, Journals@Ovid, Your Journals@Ovid; records were retained] (58); 4. limit 3 to dt=20000101-20230531 [January 1st, 2000 to May 31st, 2023] (58); 5. remove duplicates from 4 (29).
Dolutegravir	1. (dolutegravir and incidence and prevalence and resistance).af. (820); 2. limit 1 to full text [Limit not valid in Your Journals@Ovid; records were retained] (311); 3. limit 2 to (clinical trial, phase iii or meta-analysis or observational study or randomized controlled trial or "systematic review") [Limit not valid in BIOSIS Previews, Embase, Journals@Ovid, Your Journals@Ovid; records were retained] (306); 4. limit 3 to dt=20000101-20230531 [January 1st, 2000 to May 31st, 2023] (306); 5. remove duplicates from 4 (153).

Table S3. Cochrane Library, LILACS and Google Scholar search strategies

Drugs	Strategies
Integrase inhibitors	HIV Drug resistance
Bictegravir	Bictegravir resistance
Cabotegravir	Cabotegravir resistance
Dolutegravir	Dolutegravir resistance

Table S4. References obtained, depending on the source

Database	Number of references
PubMed	354
OVID	216
Cochrane Library	191
LILACS	56
Google Scholar/Google	100
Other sources	33
TOTAL	950

Table S5. Excluded references (n = 74) from the 124 full articles reviewed for eligibility, explaining the reasons for the exclusion (chronological order)

Year	First author	Reason for exclusion
2013	Eron	Raltegravir resistance
2014	Castagna	Insufficient resistance data
2014	Hurt	Prognostic factors
2015	Akil	Insufficient resistance data
2015	Stekler	Genotyping study
2016	Jiang	Insufficient resistance data
2016	Naeger	Insufficient resistance data
2016	You	Insufficient resistance data
2017	Gallant	Preliminary data study 1489
2017	Sax	Preliminary data study 1490
2018	Demarest	Insufficient resistance data
2018	Frange	Insufficient resistance data
2018	Ji	Letter
2018	Lepik	Preliminary or insufficient data
2018	Oliveira	In vitro study
2018	Rusconi	Different objective
2018	Zhang	In vivo study
2019	Acosta	Preliminary data studies 1489 and 1490
2019	Cahn	Preliminary data Viking 1 and 2
2019	Kamelian	Insufficient resistance data
2019	Kityo	Preliminary data
2019	Margot	Insufficient outcome data for DTG and BIC
2019	Modica	Pretreated and failures to INI
2019	Rhee	INI resistant
2019	Rutstein	Non-developed countries
2019	Yang	Insufficient data
2020	Andreatta	Preliminary data studies 1878 and 1844
2020	Eron	Preliminary data Viking 1 and 2
2020	Foger	Insufficient resistance data
2020	Iwuji	Clinical trial protocol
2020	Mazzuti	Insufficient outcome data for DTG and BIC
2020	Nasreddine	Insufficient data on DTG resistance
2020	Orkin	Preliminary data studies 1489 and 1490
2020	Overton	Preliminary data
2020	Rockstroh	Preliminary data
2020	Saladini	In vitro study
2020	Santoro	Genotyping study
2020	Smith	Insufficient outcome data for DTG, BIC and CAB
2021	Acosta	Insufficient data
2021	Landovitz	Insufficient data
2021	Maggiolo	Preliminary data study 4449
2021	Martin	Phenotyping study
2021	Ndashimye	Non-developed countries
2021	Patel	Insufficient data on DTG resistance
2021	Rolle	Insufficient resistance data
2021	Sax	Preliminary data
2021	Watera	Non-developed countries
2022	Ahluwalia	Prophylaxis
2022	Collins	Insufficient resistance data
2022	D'Antoni	Insufficient resistance data
2022	Delany	Insufficient data
2022	De Vito	ART utilization study
2022	Eshleman	Non-developed countries
2022	Huik	Insufficient data on DTG resistance
2022	Micán	Insufficient data
2022	Mendoza	Insufficient data on DTG resistance
2022	Nasreddine	Insufficient data
2022	Parikh	Insufficient resistance data
2022	Rhee	Genotyping studies
2022	Zhao	Insufficient outcome data for DTG, BIC and CAB
2023	Armenia	Patients with DTG failure
2023	Basso	Insufficient resistance data
2023	Cahn	Insufficient data
2023	Carlander	Different objective
2023	Compagnucci	Insufficient data on DTG resistance
2023	Fonner	Prophylaxis
2023	Havens	Insufficient data
2023	Hill	Insufficient resistance data
2023	Loosli	Pretreated and failures
2023	Mendoza	These are not emerging mutations
2023	Salvo	Insufficient data
2023	Slim	Insufficient data
2023	Shafran	Insufficient resistance data
2023	Xiao	In vitro study

SUPPLEMENT 2

Excluded references (alphabetical order) (n = 74):

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SUPPLEMENT 3

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1. Integrase inhibitors (n = 4)

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SUPPLEMENT 4

Estimation of the economic impact of virological failure (VF) associated with mutations resistance (MR) (excluding rescue ART)

There are numerous studies that analyze the cost of implementing HIV resistance testing. However, in the systematic review carried out, only 2 studies of the total cost of HIV resistance to ART were identified, whose characteristics are summarized in **Table S6**.

Table S6. Cost studies of ART resistance

References	Country (analysis year)	Method (Perspective)	Result
Krentz, 2014	Canada (2011)	Cohort study (Healthcare system)	Cost/month without resistance: CDN 1,068 Cost/month with resistance: CDN 1,396
Phillips, 2017	Sub-Saharan Africa	Model (Healthcare system)	An ART resistance rate of less than 10% would result in approximately 710,000 AIDS deaths, 380,000 new infections and an additional \$5 billion in ART costs by 2030. If ART resistance exceeds 10%, It is estimated that in 2030 there will be 890,000 deaths from AIDS, 450,000 new infections and an additional 6.5 billion dollars attributable to HIV resistance to ART.

CDN: canadian dollar; ART: antiretroviral treatment.

Due to the lack of studies on the economic impact of VF (with or without MR), A survey was conducted among the four clinical experts who co-signed this article, obtaining an estimate on the use of resources in the VF of ART (**Table S7**). It is estimated that the cost of managing VF ART in Spain would amount to €2,160 per patient (excluding the cost of possible rescue ART in cases with MR).

Table S7. Estimated resources associated with virological failure, excluding ART rescue (expert panel)

Resource	No. of resources	Unit price (€2024)	References	Cost
HIV-1 plasma viral load	7	€ 94.00	Tarifas, 2024	€ 658.00
External consultations to the specialist	6	€ 119.00	Tarifas, 2024	€ 714.00
Genotypic resistance study (GRT)	1	€ 310.50	Resolución, 2022	€ 310.50
Lymphocyte count T CD4+	1	€ 28.00	Tarifas, 2024	€ 28.00
Lymphocyte count T CD8+	1	€ 28.00	Tarifas, 2024	€ 28.00
Viral tropism	1	€ 310.50	Resolución, 2022	€ 310.50
Plasma levels of ART	1	€ 106.00	Orden, 2017	€ 106.00
Hemogram	1	€ 5.00	Tarifas, 2024	€ 5.00
Total cost, excluding rescue ART in RM				€ 2,160.00

RM: resistance mutation; ART: antiretroviral treatment.

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