



## Clinical trial results:

**Phase 3b, single arm, single site simplification study of HIV-1 infected patients with virological suppression under the combination of 3TC (150 mg BID) plus Raltegravir (400 mg BID) switching to 3TC (300 mg QD) plus Raltegravir (1200 mg QD) : Roll-over study of the RALAM clinical trial**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-000986-60 |
| Trial protocol           | ES             |
| Global end of trial date | 24 August 2020 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 09 April 2025 |
| First version publication date | 09 April 2025 |

### Trial information

#### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | RALAM-Roll-Over |
|-----------------------|-----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03311945 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                         |
|------------------------------|-------------------------------------------------------------------------|
| Sponsor organisation name    | Fundació Clinic per a la Recerca Biomèdica                              |
| Sponsor organisation address | C/ Villarroel 170, Barcelona, Spain,                                    |
| Public contact               | Judit Pich, CTU - Clinical Trials Unit, jpich@recerca.clinic.cat        |
| Scientific contact           | Dr. Esteban Martinez, Hospital Clínic de Barcelona, estebanm@clinic.cat |

Notes:

### Paediatric regulatory details

|                                                                      |    |
|----------------------------------------------------------------------|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|                                                      |                |
|------------------------------------------------------|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 24 August 2020 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 24 August 2020 |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 24 August 2020 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

Efficacy assessed with standard plasma HIV-1 RNA detection (limit of detection 50 copies/mL) at 48 weeks.

Protection of trial subjects:

This trial has a Data Monitoring Committee (DSMB). The trial will end if the DSMB reviews the data and detects 4 episodes of treatment failure, and subsequently every 4 new episodes of treatment failure. The study will be interrupted as soon as 5 episodes (10%) of confirmed virological failure are detected. Additionally, one of the principal inclusion criteria is that patients must have signed informed consent to participate in the study.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 08 May 2018 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | Yes         |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Spain: 33 |
| Worldwide total number of subjects   | 33        |
| EEA total number of subjects         | 33        |

Notes:

### Subjects enrolled per age group

|                                           |    |
|-------------------------------------------|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 33 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

#### Recruitment details:

All trial subjects were recruited at a single site in Spain: Hospital Clínic de Barcelona. The subjects were patients in the switch arm who completed the 24-week follow-up of RALAM (NCT02284035) study and remained virologically suppressed (viral load <50 copies/mL) on dual therapy with 3TC plus Raltegravir. Recruitment start period: 08-May-2018

### Pre-assignment

#### Screening details:

Selection and baseline will be done in the same visit. Performed at Week 0. During this visit, written informed consent was obtained from each patient, and demographic data, medical history, complete physical examination, and laboratory tests (including hematology, biochemistry, and plasma viral load) were performed to confirm eligibility.

### Period 1

|                              |                |
|------------------------------|----------------|
| Period 1 title               | Baseline       |
| Is this the baseline period? | Yes            |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

### Arms

|           |         |
|-----------|---------|
| Arm title | RAL+3TC |
|-----------|---------|

#### Arm description:

1200 mg raltegravir + 300 mg Lamivudine

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | ISENTRESS          |
| Investigational medicinal product code | ATC: J05AX08       |
| Other name                             | Raltegravir        |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

#### Dosage and administration details:

Dose: 1200 mg once a day (QD) during 48 weeks. It will be administered orally two 600 mg film-coated tablets of Raltegravir. Each ISENTRESS film-coated tablet contains 600 mg of raltegravir (as potassium). The rest of antiretroviral medication will be obtained through the standard prescription and dispensing route in which antiretroviral drugs are dispensed on an outpatient basis by the pharmacy service of the center.

|                                        |                              |
|----------------------------------------|------------------------------|
| Investigational medicinal product name | Epivir                       |
| Investigational medicinal product code | ATC: J05AF05                 |
| Other name                             | Lamivudine, Lamivudina (3TC) |
| Pharmaceutical forms                   | Film-coated tablet           |
| Routes of administration               | Oral use                     |

#### Dosage and administration details:

Dose: 300 mg once a day (QD) during 48 weeks. It will be administered orally one 300 mg film-coated tablet of Lamivudine.

| Number of subjects in period 1 | RAL+3TC |
|--------------------------------|---------|
| Started                        | 33      |
| Completed                      | 33      |

## Period 2

|                              |                |
|------------------------------|----------------|
| Period 2 title               | 24 weeks       |
| Is this the baseline period? | No             |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

## Arms

|                  |         |
|------------------|---------|
| <b>Arm title</b> | RAL+3TC |
|------------------|---------|

Arm description:

1200 mg raltegravir + 300 mg Lamivudine

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | ISENTRESS          |
| Investigational medicinal product code | ATC: J05AX08       |
| Other name                             | Raltegravir        |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Dose: 1200 mg once a day (QD) during 48 weeks. It will be administered orally two 600 mg film-coated tablets of Raltegravir. Each ISENTRESS film-coated tablet contains 600 mg of raltegravir (as potassium).

|                                        |                              |
|----------------------------------------|------------------------------|
| Investigational medicinal product name | Epivir                       |
| Investigational medicinal product code | ATC: J05AF05                 |
| Other name                             | Lamivudine, Lamivudina (3TC) |
| Pharmaceutical forms                   | Film-coated tablet           |
| Routes of administration               | Oral use                     |

Dosage and administration details:

Dose: 300 mg once a day (QD) during 48 weeks. It will be administered orally one 300 mg film-coated tablet of Lamivudine. The rest of antiretroviral medication will be obtained through the standard prescription and dispensing route in which antiretroviral drugs are dispensed on an outpatient basis by the pharmacy service of the center.

| Number of subjects in period 2 | RAL+3TC |
|--------------------------------|---------|
| Started                        | 33      |
| Completed                      | 31      |
| Not completed                  | 2       |
| Adverse event, non-fatal       | 2       |

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**Period 3**

|                              |                |
|------------------------------|----------------|
| Period 3 title               | 48 weeks       |
| Is this the baseline period? | No             |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

**Arms**

|                  |         |
|------------------|---------|
| <b>Arm title</b> | RAL+3TC |
|------------------|---------|

Arm description:

1200 mg raltegravir + 300 mg Lamivudine

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | ISENTRESS          |
| Investigational medicinal product code | ATC: J05AX08       |
| Other name                             | Raltegravir        |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Dose: 1200 mg once a day (QD) during 48 weeks. It will be administered orally two 600 mg film-coated tablets of Raltegravir. Each ISENTRESS film-coated tablet contains 600 mg of raltegravir (as potassium).

|                                        |                              |
|----------------------------------------|------------------------------|
| Investigational medicinal product name | Epivir                       |
| Investigational medicinal product code | ATC: J05AF05                 |
| Other name                             | Lamivudine, Lamivudina (3TC) |
| Pharmaceutical forms                   | Film-coated tablet           |
| Routes of administration               | Oral use                     |

Dosage and administration details:

Dose: 300 mg once a day (QD) during 48 weeks. It will be administered orally one 300 mg film-coated tablet of Lamivudine. The rest of antiretroviral medication will be obtained through the standard prescription and dispensing route in which antiretroviral drugs are dispensed on an outpatient basis by the pharmacy service of the center.

|                                       |         |
|---------------------------------------|---------|
| <b>Number of subjects in period 3</b> | RAL+3TC |
| Started                               | 31      |
| Completed                             | 30      |
| Not completed                         | 1       |
| Lack of efficacy                      | 1       |

## Baseline characteristics

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | RAL+3TC |
|-----------------------|---------|

Reporting group description:

1200 mg raltegravir + 300 mg Lamivudine

| Reporting group values                             | RAL+3TC | Total |  |
|----------------------------------------------------|---------|-------|--|
| Number of subjects                                 | 33      | 33    |  |
| Age categorical                                    |         |       |  |
| Units: Subjects                                    |         |       |  |
| In utero                                           |         | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) |         | 0     |  |
| Newborns (0-27 days)                               |         | 0     |  |
| Infants and toddlers (28 days-23 months)           |         | 0     |  |
| Children (2-11 years)                              |         | 0     |  |
| Adolescents (12-17 years)                          |         | 0     |  |
| Adults (18-64 years)                               |         | 0     |  |
| From 65-84 years                                   |         | 0     |  |
| 85 years and over                                  |         | 0     |  |
| Age continuous                                     |         |       |  |
| Units: years                                       |         |       |  |
| arithmetic mean                                    | 53.7    |       |  |
| standard deviation                                 | ± 12.1  | -     |  |
| Gender categorical                                 |         |       |  |
| Units: Subjects                                    |         |       |  |
| Female                                             | 7       | 7     |  |
| Male                                               | 26      | 26    |  |

## End points

### End points reporting groups

|                                                                         |         |
|-------------------------------------------------------------------------|---------|
| Reporting group title                                                   | RAL+3TC |
| Reporting group description:<br>1200 mg raltegravir + 300 mg Lamivudine |         |
| Reporting group title                                                   | RAL+3TC |
| Reporting group description:<br>1200 mg raltegravir + 300 mg Lamivudine |         |
| Reporting group title                                                   | RAL+3TC |
| Reporting group description:<br>1200 mg raltegravir + 300 mg Lamivudine |         |

### Primary: Therapeutic failure

|                                                                                                                                                                                                                     |                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| End point title                                                                                                                                                                                                     | Therapeutic failure <sup>[1]</sup> |
| End point description:<br>Therapeutic failure at week 48, includes virological failure, change in treatment for any reason, consent withdrawal, loss to follow-up or death.<br>It will be analysed also at Week 24. |                                    |
| End point type                                                                                                                                                                                                      | Primary                            |
| End point timeframe:<br>48 weeks.                                                                                                                                                                                   |                                    |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This is a single arm study.

| End point values            | RAL+3TC         |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 33              |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Yes                         | 3               |  |  |  |
| No                          | 30              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All SAEs occurring from the signing of informed consent until 30 days after receiving the last dose of the study drug were reported.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 20.0   |

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | RAL/3TC |
|-----------------------|---------|

Reporting group description:

Raltegravir 1200 mg per day plus lamivudine 300 mg per day.

| Serious adverse events                            | RAL/3TC        |  |  |
|---------------------------------------------------|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 33 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    |                |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | RAL/3TC        |  |  |
|-------------------------------------------------------|----------------|--|--|
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 3 / 33 (9.09%) |  |  |
| Blood and lymphatic system disorders                  |                |  |  |
| Dizziness, asthenia, headache                         |                |  |  |
| subjects affected / exposed                           | 1 / 33 (3.03%) |  |  |
| occurrences (all)                                     | 3              |  |  |
| Gastrointestinal disorders                            |                |  |  |
| Gastrointestinal toxicity, abdominal pain, diarrhea   |                |  |  |
| subjects affected / exposed                           | 2 / 33 (6.06%) |  |  |
| occurrences (all)                                     | 3              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/38039097>