# A phase 3 multicenter, randomised, prospective, open-label trial of fixed-duration (12 cycles) venetoclax/ obinutuzumab vs. fixed-duration (15 cycles) venetoclax/ pirtobrutinib vs. MRD-guided venetoclax/ pirtobrutinib in patients with previously untreated chronic lymphocytic leukaemia (CLL)/ small lymphocytic lymphoma (SLL) aiming to establish measurement of individual residual disease for adjustment of treatment duration to improve outcomes (CLL18/ MOIRAI)

| Estado | Tipo de Participantes | Rangos de Edad |
|---|---|---|
| Reclutando | No aportado | Mayores de 64 , Adultos (18-64 años) |
| **Género** | **Fases** | **Participantes esperados** |
| Ambos | Fase III | 67 |
| **Resultados** | **Bajo nivel intervención** | **Enfermedad rara** |
| Sin resultados | No | Si |
| **Cobertura geográfica** | **Ámbitos del ensayo** | **Terapia avanzada** |
| Sin determinar | eficacia | NO |

## Información

### Identificador
2023-510294-34-00 (CTIS)

### Cod. Protocolo
CLL18/MOIRAI

### Área terapéutica
Enfermedades [C] - Cáncer [C04]|

### Enfermedad investigada
small lymphocytic lymphoma (SLL)
chronic lymphocytic leukemia (CLL)

### Título Científico

A phase 3 multicenter, randomised, prospective, open-label trial of fixed-duration (12 cycles) venetoclax/ obinutuzumab vs. fixed-duration (15 cycles) venetoclax/ pirtobrutinib vs. MRD-guided venetoclax/ pirtobrutinib in patients with previously untreated chronic lymphocytic leukaemia (CLL)/ small lymphocytic lymphoma (SLL) aiming to establish measurement of individual residual disease for adjustment of treatment duration to improve outcomes (CLL18/MOIRAI)

## Justificación

No aportado

## Objetivo Principal

The primary objective of the study is to compare the efficacy of MRD-guided Venetoclax/Pirtobrutinib vs fixed-duration (15 cycles) Venetoclax/Pirtobrutinib and MRD-guided Venetoclax/Pirtobrutinib vs. fixed-duration (12 cycles) Venetoclax/Obinutuzumab by measuring progression-free survival (PFS) in patients with previously untreated chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL).

## Variables de Evaluación Primaria

Progression-free survival (PFS)

## Momentos temporales de evaluación primaria

No aportado

## Objetivo Secundario

To evaluate MRD levels by different types of measurement from different materials at the final restaging (three months after end of treatment) and at selected other time points
Overall response rate (ORR) as assessed by iwCLL guidelines at the final restaging (three months after end of treatment) and at selected other time points
Complete response (CR) rate as assessed by iwCLL guidelines at the final restaging (three months after end of treatment) and at selected other time points
Duration of response (DOR) as assessed by iwCLL guidelines
Time to next treatment (TTNT)
Treatment-free survival (TFS)
Overall survival (OS)
Safety and tolerability of MRD-guided Ven-Pirto, fixed-duration Ven-Pirto, and fixed-duration Ven-Obi
Best response as assessed by iwCLL guidelines until one year after end of treatment

## Variables de Evaluación Secundaria

Measurable residual disease (MRD) levels by different types of measurement from different materials at final

restaging (performed 3 months after end of treatment in all patients - except for patients that show progression of CLL disease or Richter transformation before this point of time - which differs depending on the duration of treatment) and selected other time points during and after treatment
Overall response rate (ORR) and complete response (CR) rate at the final restaging and selected other time points
Duration of response (DOR)
Time to next treatment (TTNT)
Treatment-free survival (TFS)
Overall survival (OS)
Safety parameters: Type, frequency and severity of - adverse events (AEs) -adverse events of particular interest (AEPI)
Best response assessed until 1 year after end of treatment

## Momentos temporales de evaluación secundaria

No aportado

## Criterios de Inclusión

Documented CLL/SLL requiring treatment according to iwCLL criteria with a CLL phenotype cell count >10-2 tracked by flow cytometry at screening. Adequate bone marrow function as indicated by: - an absolute neutrophil count 1 x 10/l - a hemoglobin value 8.0 g/dL without transfusions during the last 7 days unless directly attributable to CLL/SLL (e.g. bone marrow infiltration) and - a platelet count 25 x 10/l unless due to the CLL/SLL, in this case, platelet count should be 10.000/µl without transfusion during the last 7 days. Adequate renal function, as indicated by a creatinine clearance 30ml/min calculated according to the MDRD-formula or an equally accurate method (e.g. 24 hr. urine collection) Adequate liver function as indicated by: - a total bilirubin 2 x the institutional upper limit of normal (ULN) value, and - AST/ ALT 2.5 x the institutional ULN value, unless directly attributable to the patients CLL/SLL or to Gilberts Syndrome. Negative serological testing for hepatitis B (HBsAg negative and anti-HBc negative; patients positive for anti-HBc may be included if PCR for HBV DNA is negative and HBV-DNA PCR is performed every month until 12 months after last dosage of obinutuzumab), negative testing for hepatitis-C (HCV-RNA PCR) and negative HIV test within 6 weeks prior to registration Age 18 years Eastern Cooperative Oncology Group Performance Status (ECOG) performance status Life expectancy 6 months Ability and willingness to provide written informed consent and to adhere to the study visit schedule and other protocol requirements.

## Criterios de Exclusión

Any prior CLL- or SLL-specific therapies, except for corticosteroid treatment administered due to necessary immediate intervention (within the last 10 days before start of study treatment only dose equivalents up to 20 mg prednisolone per day are permitted). Fertile men or women of childbearing potential unless: - surgically sterile or 2 years after the onset of menopause, or - willing to use two methods of reliable contraception including one highly effective (Pearl Index <1) and one additional effective (barrier) method during study treatment and for the required time period thereafter (at least one and up to 18 months after end of study treatment depending of study drug(s) used, see chapter 2.2.2.1 Known risks relevant with all study drugs). Vaccination with a live vaccine 28 days prior to registration Use of investigational agents which might interfere with the study drug within 28 days prior to registration Legal incapacity Prisoners or subjects who are institutionalized by regulatory or court order Persons who are in dependence to the sponsor or an investigator Decompensated auto-immune cytopenia (defined as ongoing drop in hemoglobin (AIHA) or in platelets (ITP) in spite of prednisolone and/or intravenous immunoglobulins treatment). (Suspicion of) transformation of CLL/SLL (i.e. Richter`s transformation) or central nervous system (CNS) involvement. (Suspicion of) progressive multifocal leukoencephalopathy (PML). Malignant neoplasm other than CLL/SLL unless in remission and unlikely to adversely impact on patient´s life expectancy, defined as curatively

treated non-melanoma skin cancer or other neoplasias treated curatively 1 year ago, without signs of progression and not currently requiring systemic therapies (with the exception of ongoing anti-hormonal therapy). Active infection requiring systemic treatment, including HIV, HBV and HCV Increased risk of bleeding, e.g. due to: - known bleeding disorder - anticoagulant therapy with phenprocoumon or other vitamin K antagonists (anticoagulation with a direct oral Xa or thrombin inhibitor (DOAC) or heparin) is permitted) - major surgery 4 weeks prior to randomization - stroke or intracranial hemorrhage 6 months of randomization Any comorbidity or organ system impairment rated with a CIRS (cumulative illness rating scale) score of 4 or any other life-threatening illness, medical condition or organ system dysfunction that in the investigator´s opinion - could compromise the patient`s safety or interfere with the absorption or metabolism of the study drugs (e.g, inability to swallow tab-lets or impaired resorption in the gastrointestinal tract) Pregnant women and nursing mothers (a negative pregnancy test is required for all women of childbearing potential within 7 days before start of treatment)

# Calendario

(Última actualización: 13/07/2026)

| Autorización | Inicio de Ensayo | Inclusión Primer Paciente | Interrumpido | Reiniciado |
|---|---|---|---|---|
| 28/03/2025 | 28/11/2025 | 15/12/2025 | No aportado | No aportado |

| Fin de reclutamiento | Fin prematuro (España) | Fin prematuro (Global) | Fin del ensayo en España | Fin del ensayo global |
|---|---|---|---|---|
| No aportado | No aportado | No aportado | No aportado | No aportado |

# Promotor

### University Of Cologne Germany

**Albertus-Magnus-Platz 1**

**Contact Person**

Paula Cramer

**004922147888220**

**cll-18@uk-koeln.de**

**Monetary support: N/A**

**Tipo de promotor: Comercial**

# Ceim

### CEIM Área de Salud de Salamanca

**Pº San Vicente nº 55-182 37007 Salamanca**

**comite.etico.husa@saludcastillayleon.es**

**923291100**

# Centros

No iniciado (--/--/----)

**Complexo Hospitalario Universitario De Santiago**

Santiago De Compostela

CORUÑA

Hematology

Activo (29/04/2026)

**El Hospital Universitario De Gran Canaria Dr. Negrin**

Las Palmas De Gran Canaria

LAS PALMAS

Hematology

No iniciado (--/--/----)

**Hospital Alvaro Cunqueiro**

Vigo

PONTEVEDRA

Hematology

Activo (18/02/2026)

**Hospital Clinic De Barcelona**

Barcelona

BARCELONA

Hematology

Activo (04/12/2025)

**Hospital Clinico Universitario De Valencia**

Valencia

VALENCIA

Oncology and Hematology

Activo (08/07/2026)

**Hospital Clinico Universitario Lozano Blesa**

Zaragoza

ZARAGOZA

Hematology

Activo (01/12/2025)

**Hospital Costa Del Sol**

Marbella

MÁLAGA

Hematology and Haemotherapy

Activo (28/05/2026)

**Hospital De La Santa Creu I Sant Pau**

Barcelona

BARCELONA

Hematology

Activo (04/02/2026)

**Hospital Del Mar**

Barcelona

BARCELONA

Hematology

Activo (23/12/2025)

**Hospital General Universitario Dr. Balmis**

Alicante

ALICANTE

Hematology

No iniciado (--/--/----)

**Hospital Universitari Vall D Hebron**

Barcelona

BARCELONA

Hematology

Activo (04/02/2026)

**Hospital Universitario Central De Asturias**

Oviedo

ASTURIAS

Hematology

Activo (01/07/2026)

**Hospital Universitario De La Princesa**

Madrid

MADRID

Hematology

No iniciado (--/--/----)

**Hospital Universitario De Salamanca**

Salamanca

SALAMANCA

Hematology

Activo (05/05/2026)

**Hospital Universitario Donostia**

Donostia

GUIPÚZCOA

Hematology

Activo (15/01/2026)

**Hospital Universitario Infanta Leonor**

Madrid

MADRID

Hematology and Hemotherapy

No iniciado (--/--/----)

**Hospital Universitario La Paz**

Madrid

MADRID

Hematology

Activo (23/01/2026)

**Hospital Universitario Marques De Valdecilla**

Santander

CANTABRIA

Hematology

Activo (28/11/2025)

**Hospital Universitario Regional De Malaga**

Malaga

MÁLAGA

Hematology

No iniciado (--/--/----)

**Hospital Universitario Reina Sofia**

Cordoba

CÓRDOBA

Hematology

Activo (08/05/2026)

**Hospital Universitario Virgen De Valme**

Sevilla

SEVILLA

Hematology and Hemotherapy

Activo (12/01/2026)

**Hospital Universitario 12 De Octubre**

Madrid

MADRID

Clinical Hematology

No iniciado (--/--/----)

**Institut Catala D´oncologia**

Badalona

BARCELONA

Hematology

Activo (01/07/2026)

**Institut Catala D´oncologia**

L'hospitalet De Llobregat

BARCELONA

Hematology

Activo (27/05/2026)

**University Clinical Hospital Virgen De La Arrixaca**

Murcia

MURCIA

Hematology and Hemotherapy

# Medicamentos

**Venetoclax**
FILM-COATED TABLET
ORAL USE

-
Principios Activos: N/A

Experimental

**Venetoclax**
FILM-COATED TABLET
ORAL USE

-
Principios Activos: N/A

Experimental

**PIRTOBRUTINIB**
FILM-COATED TABLET
ORAL USE

-
Principios Activos: N/A

Experimental

**Gazyvaro 1,000 mg concentrate for solution for infusion.**
SOLUTION FOR INFUSION
INTRAVENOUS USE

Código ATC: L01XC15 - OBINUTUZUMAB
Principios Activos: N/A

Experimental

**Venetoclax**
FILM-COATED TABLET
ORAL USE

-
Principios Activos: N/A

Experimental

# Sin resultados

# A phase 3 multicenter, randomised, prospective, open-label trial of fixed-duration (12 cycles) venetoclax/ obinutuzumab vs. fixed-duration (15 cycles) venetoclax/ pirtobrutinib vs. MRD-guided venetoclax/ pirtobrutinib in patients with previously untreated chronic lymphocytic leukaemia (CLL)/ small lymphocytic lymphoma (SLL) aiming to establish measurement of individual residual disease for adjustment of treatment duration to improve outcomes (CLL18/ MOIRAI)

| State | Type of participants | Age Ranges |
|---|---|---|
| Recruiting | Not provided | Older than 64 , Adults (18-64 years) |
| **Gender** | **Phases** | **Expected Participants** |
| Both | Phase III | 67 |
| **Results** | **Low level of intervention** | **Rare disease** |
| No results | No | Yes |
| **Geographic coverage** | **Areas of the study** | **Advanced therapy** |
| Undetermined | effectiveness | NO |

## Information

### Identifier
2023-510294-34-00 (CTIS)

### Protocol Code
CLL18/MOIRAI

### Therapeutic area
Diseases [C] - Cancer [C04]|

### Investigated Disease
small lymphocytic lymphoma (SLL)
chronic lymphocytic leukemia (CLL)

### Scientific Title

A phase 3 multicenter, randomised, prospective, open-label trial of fixed-duration (12 cycles) venetoclax/ obinutuzumab vs. fixed-duration (15 cycles) venetoclax/ pirtobrutinib vs. MRD-guided venetoclax/ pirtobrutinib in patients with previously untreated chronic lymphocytic leukaemia (CLL)/ small lymphocytic lymphoma (SLL) aiming to establish measurement of individual residual disease for adjustment of treatment duration to improve outcomes (CLL18/MOIRAI)

## Rationale

Not provided

## Main Objective

The primary objective of the study is to compare the efficacy of MRD-guided Venetoclax/Pirtobrutinib vs fixed-duration (15 cycles) Venetoclax/Pirtobrutinib and MRD-guided Venetoclax/Pirtobrutinib vs. fixed-duration (12 cycles) Venetoclax/Obinutuzumab by measuring progression-free survival (PFS) in patients with previously untreated chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL).

## Primary Endpoints

Progression-free survival (PFS)

## Temporary moments of secondary assessment

Not provided

## Secondary Objective

To evaluate MRD levels by different types of measurement from different materials at the final restaging (three months after end of treatment) and at selected other time points
Overall response rate (ORR) as assessed by iwCLL guidelines at the final restaging (three months after end of treatment) and at selected other time points
Complete response (CR) rate as assessed by iwCLL guidelines at the final restaging (three months after end of treatment) and at selected other time points
Duration of response (DOR) as assessed by iwCLL guidelines
Time to next treatment (TTNT)
Treatment-free survival (TFS)
Overall survival (OS)
Safety and tolerability of MRD-guided Ven-Pirto, fixed-duration Ven-Pirto, and fixed-duration Ven-Obi
Best response as assessed by iwCLL guidelines until one year after end of treatment

## Secondary Endpoints

Measurable residual disease (MRD) levels by different types of measurement from different materials at final

restaging (performed 3 months after end of treatment in all patients - except for patients that show progression of CLL disease or Richter transformation before this point of time - which differs depending on the duration of treatment) and selected other time points during and after treatment
Overall response rate (ORR) and complete response (CR) rate at the final restaging and selected other time points
Duration of response (DOR)
Time to next treatment (TTNT)
Treatment-free survival (TFS)
Overall survival (OS)
Safety parameters: Type, frequency and severity of - adverse events (AEs) -adverse events of particular interest (AEPI)
Best response assessed until 1 year after end of treatment

## Temporary moments of secondary assessment

Not provided

## Inclusion criteria

Documented CLL/SLL requiring treatment according to iwCLL criteria with a CLL phenotype cell count >10-2 tracked by flow cytometry at screening. Adequate bone marrow function as indicated by: - an absolute neutrophil count 1 x 10/l - a hemoglobin value 8.0 g/dL without transfusions during the last 7 days unless directly attributable to CLL/SLL (e.g. bone marrow infiltration) and - a platelet count 25 x 10/l unless due to the CLL/SLL, in this case, platelet count should be 10.000/µl without transfusion during the last 7 days. Adequate renal function, as indicated by a creatinine clearance 30ml/min calculated according to the MDRD-formula or an equally accurate method (e.g. 24 hr. urine collection) Adequate liver function as indicated by: - a total bilirubin 2 x the institutional upper limit of normal (ULN) value, and - AST/ ALT 2.5 x the institutional ULN value, unless directly attributable to the patients CLL/SLL or to Gilberts Syndrome. Negative serological testing for hepatitis B (HBsAg negative and anti-HBc negative; patients positive for anti-HBc may be included if PCR for HBV DNA is negative and HBV-DNA PCR is performed every month until 12 months after last dosage of obinutuzumab), negative testing for hepatitis-C (HCV-RNA PCR) and negative HIV test within 6 weeks prior to registration Age 18 years Eastern Cooperative Oncology Group Performance Status (ECOG) performance status Life expectancy 6 months Ability and willingness to provide written informed consent and to adhere to the study visit schedule and other protocol requirements.

## Exclusion criteria

Any prior CLL- or SLL-specific therapies, except for corticosteroid treatment administered due to necessary immediate intervention (within the last 10 days before start of study treatment only dose equivalents up to 20 mg prednisolone per day are permitted). Fertile men or women of childbearing potential unless: - surgically sterile or 2 years after the onset of menopause, or - willing to use two methods of reliable contraception including one highly effective (Pearl Index <1) and one additional effective (barrier) method during study treatment and for the required time period thereafter (at least one and up to 18 months after end of study treatment depending of study drug(s) used, see chapter 2.2.2.1 Known risks relevant with all study drugs). Vaccination with a live vaccine 28 days prior to registration Use of investigational agents which might interfere with the study drug within 28 days prior to registration Legal incapacity Prisoners or subjects who are institutionalized by regulatory or court order Persons who are in dependence to the sponsor or an investigator Decompensated auto-immune cytopenia (defined as ongoing drop in hemoglobin (AIHA) or in platelets (ITP) in spite of prednisolone and/or intravenous immunoglobulins treatment). (Suspicion of) transformation of CLL/SLL (i.e. Richter`s transformation) or central nervous system (CNS) involvement. (Suspicion of) progressive multifocal leukoencephalopathy (PML). Malignant neoplasm other than CLL/SLL unless in remission and unlikely to adversely impact on patient´s life expectancy, defined as curatively

treated non-melanoma skin cancer or other neoplasias treated curatively 1 year ago, without signs of progression and not currently requiring systemic therapies (with the exception of ongoing anti-hormonal therapy). Active infection requiring systemic treatment, including HIV, HBV and HCV Increased risk of bleeding, e.g. due to: - known bleeding disorder - anticoagulant therapy with phenprocoumon or other vitamin K antagonists (anticoagulation with a direct oral Xa or thrombin inhibitor (DOAC) or heparin) is permitted) - major surgery 4 weeks prior to randomization - stroke or intracranial hemorrhage 6 months of randomization Any comorbidity or organ system impairment rated with a CIRS (cumulative illness rating scale) score of 4 or any other life-threatening illness, medical condition or organ system dysfunction that in the investigator´s opinion - could compromise the patient`s safety or interfere with the absorption or metabolism of the study drugs (e.g, inability to swallow tab-lets or impaired resorption in the gastrointestinal tract) Pregnant women and nursing mothers (a negative pregnancy test is required for all women of childbearing potential within 7 days before start of treatment)

# Calendar

(Last Update: 13/07/2026)

| Authorization | Start of Trial | First patient inclusion | Halted | Restarted |
|---|---|---|---|---|
| 28/03/2025 | 28/11/2025 | 15/12/2025 | Not aported | Not aported |

| End of recruitment | Premature end (Spain) | Premature End (Global) | Trial end (Spain) | Trial end (Global) |
|---|---|---|---|---|
| Not aported | Not aported | Not aported | Not aported | Not aported |

# Sponsor

**University Of Cologne Germany**

**Albertus-Magnus-Platz 1**

**Contact Person**

Paula Cramer

**004922147888220**

**cll-18@uk-koeln.de**

**Monetary support: N/A**

**Sponsor type: Commercial**

# Ceim

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**Pº San Vicente nº 55-182 37007 Salamanca**

**comite.etico.husa@saludcastillayleon.es**

**923291100**

# Sites

not initialized (--/--/----)

**Complexo Hospitalario Universitario De Santiago**

Santiago De Compostela

CORUÑA

Hematology

Active (29/04/2026)

**El Hospital Universitario De Gran Canaria Dr. Negrin**

Las Palmas De Gran Canaria

LAS PALMAS

Hematology

not initialized (--/--/----)

**Hospital Alvaro Cunqueiro**

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**Hospital Clinico Universitario Lozano Blesa**

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ZARAGOZA

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**Hospital Costa Del Sol**

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MÁLAGA

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**Hospital De La Santa Creu I Sant Pau**

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**Hospital Universitari Vall D Hebron**

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**Hospital Universitario Central De Asturias**

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**Hospital Universitario De La Princesa**

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not initialized (--/--/----)

**Hospital Universitario De Salamanca**

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**Hospital Universitario Donostia**

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Active (15/01/2026)

**Hospital Universitario Infanta Leonor**

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Hematology and Hemotherapy

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**Hospital Universitario La Paz**

Madrid

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**Hospital Universitario Marques De Valdecilla**

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CANTABRIA

Hematology

Active (28/11/2025)

**Hospital Universitario Regional De Malaga**

Malaga

MÁLAGA

Hematology

not initialized (--/--/----)

**Hospital Universitario Reina Sofia**

Cordoba

CÓRDOBA

Hematology

Active (08/05/2026)

**Hospital Universitario Virgen De Valme**

Sevilla

SEVILLA

Hematology and Hemotherapy

Active (12/01/2026)

**Hospital Universitario 12 De Octubre**

Madrid

MADRID

Clinical Hematology

not initialized (--/--/----)

**Institut Catala D´oncologia**

Badalona

BARCELONA

Hematology

Active (01/07/2026)

**Institut Catala D´oncologia**

L'hospitalet De Llobregat

BARCELONA

Hematology

Active (27/05/2026)

**University Clinical Hospital Virgen De La Arrixaca**

Murcia

MURCIA

Hematology and Hemotherapy

# Medication

**Venetoclax**
FILM-COATED TABLET
ORAL USE

-
Active Principles: N/A

Experimental

**Venetoclax**
FILM-COATED TABLET
ORAL USE

-
Active Principles: N/A

Experimental

**PIRTOBRUTINIB**
FILM-COATED TABLET
ORAL USE

-
Active Principles: N/A

Experimental

**Gazyvaro 1,000 mg concentrate for solution for infusion.**
SOLUTION FOR INFUSION
INTRAVENOUS USE

ATC code: L01XC15 - OBINUTUZUMAB
Active Principles: N/A

Experimental

**Venetoclax**
FILM-COATED TABLET
ORAL USE

-
Active Principles: N/A

Experimental

# No results