# A Phase II, open-label trial to evaluate the safety, tolerability and antiviral activity of TMC125 in antiretroviral experienced HIV-1 infected children and adolescents.

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This study is a Phase II, non-randomized, open label trial to evaluate Safety and Antiviral activity of Etravirine (TMC125) in Treatment-Experienced, HIV Infected Children and Adolescents.

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Viral infectious disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON31931

**Source**
ToetsingOnline

**Brief title**
PIANO = Pediatric trial with Intelence as an Active NNRTI Option

### Condition

- Viral infectious disorders

**Synonym**
AIDS, HIV-infection

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Janssen-Cilag
**Source(s) of monetary or material Support:** de opdrachtgever van het onderzoek

## Intervention

**Keyword:** HIV-infected, NNRTI, pediatric, TMC125

## Outcome measures

### Primary outcome

The primary objective is long-term safety and tolerability of TMC125 in

combination with other HIV drugs [ Time Frame: 24 weeks ]

### Secondary outcome

The secondary objectives are pharmacokinetic parameters throughout the study,

HIV viral load, CD4 count and percentage, Genotypic and phenotypic resistance

measures [ Time Frame: 48 week ]

# Study description

### Background summary

Etravirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI). In adults, etravirine has shown significant antiretroviral activity in clinical trials and is generally safe and well tolerated. However, there is no data on the drug's long-term safety and antiviral activity in children and adolescents.

HIV-1 infection in the pediatric population follows a similar course as seen in adult HIV-1
infection. However, pediatric HIV infection presents considerable challenges due to the
differences in epidemiology and transmission, diagnostic challenges, clinical manifestations, and
management. Control of HIV replication is the goal of treatment in both children and adults.
Recent trials of antiretroviral combination therapy in infants and children have provided an

improved understanding of the pathogenesis of pediatric human immunodeficiency virus-type 1
(HIV-1) infection. Currently, highly active combination regimens including at least 3 drugs are
recommended. Such regimens have been associated with enhanced survival, reduction in
opportunistic infections and other complications of HIV infection, and improved quality of life in
children.

Not all ARVs approved in adults are available for children.
Of the 4 NNRTIs currently available, 2 (nevirapine [NVP] and efavirenz [EFV]) have an approved pediatric indication. Development of new, potent antiretroviral (ARV)
compounds with different and improved resistance and safety profiles remains a high unmet need
especially in treatment experienced HIV-1 infected pediatric population. In addition to the need
for new ARVs, the treatment of HIV-1 infected pediatric subjects has to take into account
clinical care issues that are unique to this population such as age-related differences in virologic,
immunologic, and pharmacokinetic parameters and obstacles associated with adherence to
complex regimens.

**Study objective**

This study is a Phase II, non-randomized, open label trial to evaluate Safety and Antiviral activity of Etravirine (TMC125) in Treatment-Experienced, HIV Infected Children and Adolescents.

**Study design**

This study will last for a maximum of 48 weeks and will enroll participants aged 6 to 17 years. A total of 100 participants will receive etravirine tablets based on body weight and an investigator selected OBR of at least 2 antiretrovirals (ARVs), consisting of a boosted protease inhibitor (PI) and nucleoside reverse transcriptase inhibitor(s) (NRTI[s]). Use of enfuvirtide is optional.
The TMC125 dose will be based on body weight. TMC125 tablets will be provided as 25mg and 100mg.

**Intervention**

The OBR will be composed at the discretion of the investigator and should

consist of a regimen of at least 2 ARV drugs (not counting low dose ritonavir), including a boosted PI in combination with N(t)RTI(s). Additional use of ENF is optional. All ARVs for which pediatric dosing guidelines have been established with adequate safety information and for which co-administration with TMC125 is allowed can be used. ATV/rtv may be used after discussion with the Sponsor. However, the OBR may not contain an NNRTI, or any disallowed ARVs. ARVs that are not yet labeled for use in the pediatric population but
where dosing recommendations are available based on clinical data may be used after discussion with the Sponsor.
For all subjects entering the trial, results of the screening resistance test (virco®TYPE HIV-1) should be used together with the treatment history to select the OBR. The OBR should contain at least 2 active ARV drugs. In case of ENF use, ENF is considered sensitive if it has not previously been used.
Sensitivity for TMC125 will be determined using the most recent resistance algorithm. An up to date resistance interpretation will be provided to the investigator and can be used to determine eligibility in the trial.
On the baseline visit (Day 1), all subjects will be treated with TMC125, in combination with the OBR. The TMC125 dose will be based on body weight.

**Study burden and risks**

Burden is the visit frequency per protocol and blood sampling procedures, over a period of 58 weeks in total.

Risks are the risks associated with the commercial OBR therapies and risks of TMC125 (and TMC114 if applicable) described in the Informed Consent Forms.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

## Inclusion criteria

Children and adolescents aged 6 years to 17 years inclusive
Both male and female patients
HIV-1 infected
Body weight according to age within the 10-90th percentile of CDC growth chart
On steady antiretroviral therapy regimen for at least 8 weeks at screening and willing to remain on that regimen until baseline
HIV viral load of 500 copies/ml or greater at study entry
Parent or legal guardian willing to provide informed consent, if necessary

## Exclusion criteria

Evidence of resistance to etravirine
Any grade 3 or 4 toxicity (More information available in the protocol)
Use of disallowed concomitant therapy (specified in the protocol)
Currently active AIDS defining illness (category C)
Active hepatitis A, B or C virus infection
Any clinically significant diseases or findings that, in the opinion of the investigator, would interfere with the study
Receipt of any ARV or non-ARV investigational medication or investigational vaccine within 30 days prior to screening
History of clinically significant allergy or hypersensitivity to any of the excipients of the investigational medication (TMC125)

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-09-2008 |
| Enrollment: | 2 |
| Type: | Anticipated |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Intelence |
| Generic name: | Etravirine |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Prezista |
| Generic name: | Darunavir |
| Registration: | Yes - NL intended use |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 01-08-2008 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 09-09-2008 |

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| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 18-11-2008 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 13-01-2009 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-02-2009 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 25-03-2009 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-04-2009 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-11-2009 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-12-2009 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2007-007086-21-NL |
| ClinicalTrials.gov | NCT00665847 |
| CCMO | NL23759.029.08 |