EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 August 2010
EMA/150112/2013
Committee for Medicinal Products for Human Use (CHMP)

Intelence

(etravirine)

Procedure No. EMEA/H/C/000900/P46/0029

CHMP assessment report for paediatric use studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Assessment Report as adopted by the CHMP with all information of a commercially confidential nature deleted

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

1. INTRODUCTION

In accordance with Article 46 of Regulation (EC) N° 1901/2006, Tibotec, on behalf of the MAH Janssen-Cilag International, is submitting the final report for trial TMC125-C126, a Phase I, open-label trial to investigate the pharmacokinetics, safety and tolerability of TMC125 at steady state in treatment-experienced HIV-infected children. The study is also part of the follow-up measure FUM C013.

Of note, the same information was submitted in 2008 to the Pediatric Committee as part of the Pediatric Implementation Plan and in March 2009 to the Article 46-mailbox of the EMEA.

Trial TMC125-C126 is part of a clinical development program. The variation application consisting of the full relevant data package (i.e. containing several studies) is expected to be submitted by 4Q2011, as indicated in the recent PIP.

The MAH stated that in accordance with Article 16(2) of Regulation (EC) N° 726/2004, the data submitted do not influence the benefit-risk balance for INTELENCE and therefore do not require to take further regulatory action on the marketing authorization for INTELENCE at this stage.

2. SCIENTIFIC DISCUSSION

2.1. Introduction

Etravirine (ETR, INTELENCE) belongs to the class of non-nucleoside reverse transcriptase inhibitor (NNRTI) drugs and is administered via the oral route of administration. ETR, in combination with other antiretroviral medicinal products, is indicated for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in antiretroviral treatment-experienced adult patients, including those with NNRTI resistance.

The objective of this clinical overview is to support the submission of the pediatric clinical data from trial TMC125-C126 in accordance with Art 46 from Regulation N° 1901/2006.

2.2. Study TMC125-C126

2.2.1. Description of the study

Trial TMC125-C126 was the initial step in the pediatric program to evaluate the efficacy and safety of etravirine in children and adolescents.

This was a Phase I, open-label, dose-ranging trial to evaluate pharmacokinetics, and short-term safety and tolerability of etravirine at steady-state in HIV-1 infected children who are virologically suppressed. The trial has been conducted to obtain dose recommendations of etravirine per body weight in treatment-experienced HIV-1 infected children ≥ 6 years old and weighing ≥ 20 kg. Etravirine was administered as formulation F060 (100 mg tablet) and/or as formulation F066 (25 mg tablet).

The trial population comprised of subjects taking a stable ARV regimen that included lopinavir/ritonavir (LPV/rtv) and a minimum of 2 NRTIs, with or without enfuvirtide (ENF).

Trial TMC125-C126 was conducted in two sequential stages, in Stage I the dose of etravirine was 4 mg/kg b.i.d. and in Stage II the dose of etravirine was 5.2 mg/kg b.i.d. (representing a 30% increase from 4 mg/kg b.i.d.). In each Stage, at least 20 virologically suppressed (Viral Load < 50 copies/ml) children on a LPV/rtv containing regimen received etravirine for 7 days followed by an intensive 12-hour pharmacokinetic assessment of etravirine on Day 8.

The primary objective of trial TMC125-C126 was to achieve comparable pharmacokinetics in children as in adults.

Trial TMC125-C228 was chosen as the protocol-specified reference for TMC125-C126 since, at the time, it provided the pharmacokinetic parameters and associated variability of TMC125 administered as formulation F060, 200 mg b.i.d. in treatment-experienced HIV-1 infected adults who were currently receiving a boosted PI (primarily LPV/rtv).

During the conduct of Stage 2 of this Phase I trial TMC125-C126, results from the Phase III trials, DUET-1 and -2, became available demonstrating the efficacy, safety and tolerability of TMC125 in adults over 48 weeks. Results of these studies were also taken into account for analysis.

2.2.1.1. Statistical Methods

The objective of the trial was to show that the pharmacokinetics in children were in the range of the exposures of adults. This was evaluated according to the following criterion: the mean values of the exposure (expressed as AUC12h) and of Cmin had to fall within the 80 to 125% of the mean exposure and Cmin in adults (mean AUC12h = 3713 ng.h/mL, mean Cmin of 184.7 ng/mL). It was assumed that the variability between children was the same as between adults (standard deviation [SD] AUC12h = 2069 ng.h./mL, SD Cmin = 128.1 ng/mL).

If subjects discontinued the trial before receiving their first dose of study medication, additional subjects could be recruited to have 10 subjects in each age group starting treatment in each stage. If more than 2 subjects per age group were prematurely (before treatment completion) withdrawn from the trial after starting treatment for reasons other than drug tolerability/safety, additional subjects were recruited to aim for at least 8 evaluable subjects per age group. An evaluable subject was a subject who had completed an entire treatment period for the stage in which they were enrolled.

2.2.1.2. Pharmacokinetic Parameter Analysis

Based on the individual plasma concentration-time data, using the scheduled sampling times, the following pharmacokinetic parameters were derived from the bioanalytical results: **For TMC125**: On Day 8 of Stage 1 and Stage 2: C0h, Cmin, Cmax, tmax, AUC12h, Css,av, and Fl Ind

2.2.2. Results

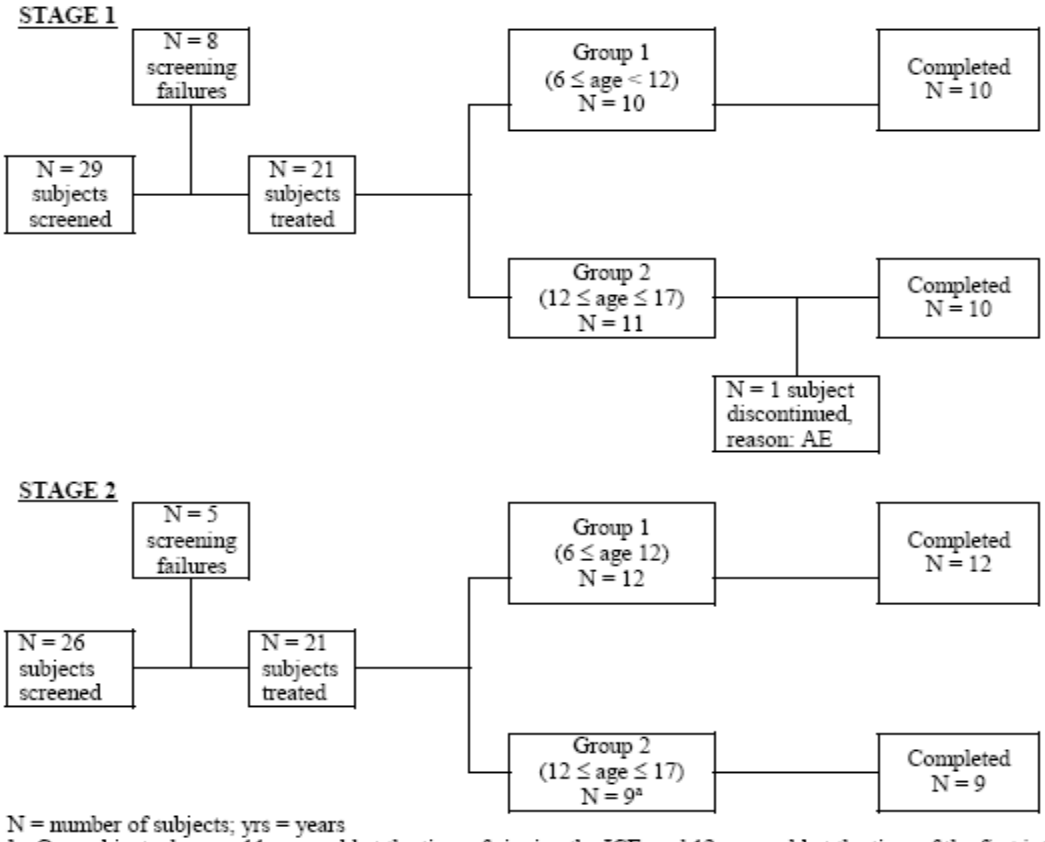
2.2.2.1. Subjects and treatment information

- **Overview**

A total of 29 subjects were screened for Stage 1 of this trial.

An interim analysis of the pharmacokinetic and safety data of this dose, performed when 17 subjects completed (or prematurely discontinued) the trial, revealed a pharmacokinetic exposure comparable to that seen in a Phase I trial in HIV-1 infected adults, and no major safety or tolerability concerns.

A total of 26 subjects were screened for Stage 2.



N = number of subjects; yrs = years

[a] One subject who was 11 years old at the time of signing the ICF, and 12 years old at the time of the first intake of study medication, was included in Group 1.

Subjects were on an individually selected ARV regimen including LPV/rtv and a minimum of 2 NRTIs, with or without ENF. Study medication in Stages 1 and 2 consisted of TMC125 4 mg/kg b.i.d. or 5.2 mg/kg b.i.d., respectively, for 7 days with an additional morning dose on Day 8.

Source: Display GEN.4 and Display GEN.5

Figure 1: Subject Disposition in Trial TMC125-TiDP02-C126

- **Baseline characteristics**

There were no relevant differences between the 2 stages with respect to demographic and baseline characteristics.

Table 7: Demographic Data

Parameter	Stage 1 Group 1 (≥ 6 to < 12 years old) N = 10	Stage 1 Group 2 (≥ 12 to ≤ 17 years old) N = 11	Stage 1 All subjects[a] N= 21	Stage 2 Group 1 (≥ 6 to < 12 years old) N = 12	Stage 2 Group 2 (≥ 12 to ≤ 17 years old) N = 9	Stage 2 All subjects[a] N= 21
Age, years Median (range)	8.5 (6-11)	13.0 (12-17)	12.0 (6-17)	9.5 (7-11)	14.0 (12-17)	10.0 (7-17)
Height, cm Median (range)	129.0 (120-148)	161.0 (152-180)	152.0 (120-180)	135.0 (117-155)	158.0 (152-179)	143.0 (117-179)
Weight, kg Median (range)	25.5 (20-43)	52.7 (39-65)	39.0 (20-65)	30.0 (22-48)	54.0 (38-63)	38.0 (22-63)
BSA, m^2 Median (range)	0.95 (0.8-1.3)	1.50 (1.3-1.7)	1.30 (0.8-1.7)	1.10 (0.8-1.4)	1.50 (1.3-1.7)	1.3 (0.8-1.7)
Sex, n (%)						
Male	6 (60.0)	7 (63.6)	13 (61.9)	4 (33.3)	4 (44.4)	8 (38.1)
Female	4 (40.0)	4 (36.4)	8 (38.1)	8 (66.7)	5 (55.6)	13 (61.9)
Ethnic Origin, n (%)						
Caucasian	7 (70.0)	6 (54.5)	13 (61.9)	5 (41.7)	5 (55.6)	10 (47.6)
Black	1 (10.0)	4 (36.4)	5 (23.8)	5 (41.7)	4 (44.4)	9 (42.9)
Hispanic	1 (10.0)	0	1 (4.8)	2 (16.7)	0	2 (9.5)
Other	1 (10.0)	1 (9.1)	2 (9.5)	0	0	0

[a] Seven subjects (3 subjects in Group 1 and 4 subjects in Group 2) participated in both Stage 1 and 2 of this trial.
N = total number of subjects, n = number of observations
Source: Display GEN.2

Table 8: Baseline Disease Characteristics

Parameter	Stage 1 Group 1 (≥ 6 to < 12 years old) N = 10	Stage 1 Group 2 (≥ 12 to ≤ 17 years old) N = 11	Stage 1 All subjects N= 21	Stage 2 Group 1 (≥ 6 to < 12 years old) N = 12	Stage 2 Group 2 (≥ 12 to ≤ 17 years old) N = 9	Stage 2 All subjects N= 21
CD4+ count (x 10^6 cells/L), Median (range)	951 (533-1553)	851 (233-1294)	887 (233-1553)	773 (493-1175)	702 (223-974)	718 (223-1175)
CD4+ count %, Median (range)	37.4 (26.8-43.3)	37.3 (25.4-46.2)	37.3 (25.4-46.2)	35.2 (28.7-40.7)	36.7 (20.3-49.0)	35.3 (20.3-49.0)
Duration since HIV diagnosis, years Median (range)	8.2 (4.9-10.7)	11.1 (0.8-15.2)	9.2 (0.8-15.2)	8.9 (3.8-11.7)	12.7 (3.0-17.8)	10.4 (3.0-17.8)
Mode of HIV infection, n (%)						
Mother to child transmission	9 (90.0)	11 (100.0)	20 (95.2)	12 (100.0)	9 (100.0)	21 (100.0)
Unknown	1 (10.0)	0	1 (4.8)	0	0	0

N = total number of subjects; n = number of subjects with observations
[a] Imputed with the last available screening value if the baseline value is missing.
Source: Display GEN.3 and Display SAF.14

- **Antiretroviral therapy**

All subjects were on a stable regimen of LPV/rtv and at least 2 NRTIs, with or without ENF, at approved pediatric doses for at least 2 months prior to screening until at least 7 days after the last intake of study medication.

None of the subjects used enfuvirtide as part of their ARV regimen.

In Stage 1, the most commonly used NRTIs were lamivudine (61.9%), abacavir (33.3%), zidovudine (33.3%), and didanosine (28.6%). In Stage 2, the most commonly used NRTIs were lamivudine (61.9%), zidovudine (33.3%), didanosine (28.6%) and abavacir (sulphate) (28.6%).

One subject (Stage 2, Group 1) used an NNRTI (i.e., efavirenz) in combination with the allowed OBR (LPV/rtv and NRTIs). This was captured as a protocol major violation under disallowed ARVs.

2.2.2.2. Pharmacocinetic results

- **Pharmacokinetics of TMC125**

A summary list of key pharmacokinetic parameters of TMC125 for Stage 1 and 2 are presented in table 10 below:

Table 10: Pharmacokinetic Results of TMC125 After Administration of TMC125 4 mg/kg b.i.d. (Stage 1) and After Administration of TMC125 5.2 mg/kg b.i.d. (Stage 2)

Pharmacokinetics of TMC125 (mean ± SD, t_{max}: median [range])	4 mg/kg TMC125 b.i.d. children and adolescents (Stage 1)	5.2 mg/kg TMC125 b.i.d. children and adolescents (Stage 2)
n	19[a]	20
C_{0h}, ng/mL	206.5 ± 145.4	360.3 ± 351.9
C_{min}, ng/mL	183.5 ± 150.6	294.3 ± 277.8
C_{max}, ng/mL	495.3 ± 453.2	756.6 ± 680.4
t_{max}, h	4.00 (2.00 - 8.00)	3.95 (2.00 - 6.07)
AUC_{12h}, ng.h/mL	4050 ± 3602	6141 ± 5586
$C_{ss,av}$, ng/mL	338.2 ± 299.4	513.0 ± 465.1
Fl Ind, %	96.82 ± 31.57	95.64 ± 26.41

[a] n=18 for AUC_{12h}, $C_{ss,av}$ and Fl Ind

The statistical results comparing Cmin and AUC12h from Stage 1 and 2 versus Cmin and AUC12h obtained in HIV-1 infected, treatment experienced adults from the TMC125-C228 trial are presented in table 11 and 12 below:

Table 11: Summary of the Statistical Analysis of the Pharmacokinetic Parameters of TMC125 After Administration of TMC125 4 mg/kg b.i.d. in Children and Adolescents (Stage 1) and Historical Adult Data of the TMC125-C228 Trial

Parameter	LSmeans [a]		LSmeans ratio, %	90% CI,% [b]
	TMC125 200 mg b.i.d. adults (reference)	TMC125 4 mg/kg b.i.d. children and adolescents (test)		
C_{min}, ng/mL	142.2	140.1	98.51	67.00 - 144.8
AUC_{12h}, ng.h/mL	3125	3171	101.5	72.76 - 141.6

[a] n=27 for Reference; n=19 for Test C_{min} and n=18 for Test AUC_{12h}
[b] 90% confidence intervals.

Based on the ratios of the LSmeans, Cmin and AUC12h of TMC125 were comparable when TMC125 was administered as 4 mg/kg b.i.d. to children or administered as TMC125 200 mg b.i.d. to adults in trial TMC125-C228.

Table 12: Summary of the Statistical Analysis of the Pharmacokinetic Parameters of TMC125 After Administration of TMC125 5.2 mg/kg b.i.d. in Children and Adolescents (Stage 2) and Historical Adult Data of the TMC125-C228 Trial

Parameter	LSmeans [a]		LSmeans ratio, %	90% CI,% [b]
	TMC125 200 mg b.i.d. adults (reference)	TMC125 5.2 mg/kg b.i.d. children and adolescents (test)		
C_{min}, ng/mL	142.2	224.3	157.7	109.3 - 227.7
AUC_{12h}, ng.h/mL	3125	4946	158.3	116.3 - 215.4

[a] n=27 for Reference; n=20 for Test

[b] 90% confidence intervals.

Based on the ratios of the LSmeans, Cmin and AUC12h of TMC125 were increased by 58% when TMC125 was administered as 5.2 mg/kg b.i.d. to children compared to administration of 200 mg b.i.d. to adults in trial TMC125-C228.

- **Pharmacokinetics of TMC125 discussed by Age Group**

A summary list of key pharmacokinetic parameters of TMC125 both stages and separated by age group are presented in table 13 below:

Table 13: Pharmacokinetic Results of TMC125 After Administration of TMC125 4 mg/kg b.i.d. (Stage 1) and After Administration of 5.2 mg/kg TMC125 b.i.d. (Stage 2), Separated by age Group

Pharmacokinetics of TMC125 (mean ± SD, t_{max}: median [range])	4 mg/kg TMC125 b.i.d. children and adolescents (Stage 1)		5.2 mg/kg TMC125 b.i.d. children and adolescents (Stage 2)	
	≥ 6 to < 12 years old	≥ 12 to ≤ 17 years old	≥ 6 to < 12 years old	≥ 12 to ≤ 17 years old
n	9[a]	10	11	9
C_{0h}, ng/mL	238.1 ± 202.4	178.0 ± 63.23	453.3 ± 441.6	246.7 ± 154.6
C_{min}, ng/mL	208.6 ± 210.1	160.8 ± 70.16	362.8 ± 351.7	210.5 ± 119.8
C_{max}, ng/mL	597.9 ± 634.8	402.9±180.5	971.1 ± 866.4	494.3 ± 144.0
t_{max}, h	4.02 (2.83 - 8.00)	4.00 (2.00 - 6.02)	4.00 (2.00 - 6.07)	3.92 (2.98 - 6.00)
AUC_{12h}, ng.h/mL	4989 ± 5189	3299 ± 1468	7713 ± 7160	4219 ± 1575
$C_{ss,av}$, ng/mL	416.3 ± 431.3	275.8± 121.8	644.3 ± 595.7	352.6 ± 132.6
Fl Ind, %	107.9 ± 44.09	87.97 ± 13.23	102.9 ± 24.98	86.79 ± 26.75

[a] n=8 for AUC_{12h}, $C_{ss,av}$ and Fl Ind

The statistical results comparing Cmin and AUC12h from the age groups in Stage 1 and 2 versus the Cmin and AUC12h obtained in HIV-infected, treatment experienced adults from the TMC125-C228 trial are presented in table 14 to table 17 below:

Table 14: Summary of the Statistical Analysis of the Pharmacokinetic Parameters of TMC125 After Administration of TMC125 4 mg/kg b.i.d. in Children Aged Between 6 and 12 (Stage 1) and Historical Adult Data of the TMC125-C228 Trial

Parameter	LSmeans [a]		LSmeans ratio, %	90% CI,% [b]
	TMC125 200 mg b.i.d. adults (reference)	TMC125 4 mg/kg b.i.d. children ≥ 6 to <12 years old (test)		
C_{min}, ng/mL	142.2	132.2	92.93	53.75 - 160.7
AUC_{12h}, ng.h/mL	3125	3373	108.0	66.81 - 174.4

[a] n=27 for Reference; n=9 for Test C_{min} and n=8 for Test AUC_{12h}

[b] 90% confidence intervals.

Table 15: Summary of the Statistical Analysis of the Pharmacokinetic Parameters of TMC125 After Administration of TMC125 4 mg/kg b.i.d. in Adolescents Aged Between 12 and 17 years old (Stage 2) and Historical Adult Data of the TMC125-C228 Trial

Parameter	LSmeans [a]		LSmeans ratio, %	90% CI,% [b]
	TMC125 200 mg b.i.d. adults (reference)	TMC125 4 mg/kg b.i.d. adolescents ≥ 12 to ≤17 years old (test)		
C_{min}, ng/mL	142.2	147.7	103.8	66.81 - 161.3
AUC_{12h}, ng.h/mL	3125	3019	96.62	66.67 - 140.0

[a] n=27 for Reference; n=10 for Test
[b] 90% confidence intervals.

Based on the ratios of the LSmeans, Cmin and AUC12h of TMC125 were, independent of age group, comparable when TMC125 was administered as 4 mg/kg b.i.d. to children or administered as TMC125 200 mg b.i.d. to adults in trial TMC125-C228.

Table 16: Summary of the Statistical Analysis of the Pharmacokinetic Parameters of TMC125 After Administration of TMC125 5.2 mg/kg b.i.d. in Children Aged Between 6 and 12 (Stage 2) and Historical Adult Data of the TMC125-C228 Trial

Parameter	LSmeans [a]		LSmeans ratio, %	90% CI,% [b]
	TMC125 200 mg b.i.d. adults (reference)	TMC125 5.2 mg/kg b.i.d. children ≥ 6 to <12 years old (test)		
C_{min}, ng/mL	142.2	260.8	183.4	114.2 – 294.3
AUC_{12h}, ng.h/mL	3125	5950	190.4	128.5 – 282.1

[a] n=27 for Reference; n=11 for Test
[b] 90% confidence intervals.

Table 17: Summary of the Statistical Analysis of the Pharmacokinetic Parameters of TMC125 After Administration of 5.2 mg/kg TMC125 b.i.d. in Adolescents Aged Between 12 and 17 (Stage 2) and Historical Adult Data of the TMC125-C228 Trial.

Parameter	LSmeans [a]		LSmeans ratio, %	90% CI,% [b]
	TMC125 200 mg b.i.d. adults (reference)	TMC125 5.2 mg/kg b.i.d. adolescents ≥ 12 to ≤17 years old (test)		
C_{min}, ng/mL	142.2	186.6	131.2	82.03 - 209.9
AUC_{12h}, ng.h/mL	3125	3946	126.3	86.03 - 185.3

[a] n=27 for Reference; n=9 for Test
[b] 90% confidence intervals.

Based on the ratios of the LSmeans, Cmin and AUC12h of TMC125 were increased by, 83% and 90%, respectively when TMC125 was administered as 5.2 mg/kg b.i.d. to children ≥ 6 and < 12 years old compared to administration of 200 mg b.i.d. to adults in trial TMC125-C228.

The LSmeans ratio of Cmin and AUC12h were increased by respectively 31% and 26% when TMC125 was administered as 5.2 mg/kg b.i.d. to adolescents ≥ 12 and ≤ 17 years old compared to administration of 200 mg b.i.d. in adults.

- **Pharmacokinetics conclusions**

Comparing both age groups within Stage 1 (4 mg/kg b.i.d.) in this trial to HIV-1 infected, treatment-experienced adults showed that Cmin and AUC12h were independent of age group.

However, when TMC125 was administered as 5.2 mg/kg b.i.d. in children and adolescents, higher Cmin and AUC12h values were observed compared to administration of TMC125 as 200 mg b.i.d. in adults (increases by 83% and 90%, respectively, in Group 1 and 31% and 26%, respectively, in Group 2).

The results of this trial showed that the exposures achieved with the 5.2 mg/kg b.i.d. dose were comparable to those seen in adults participating in the DUET trials [(The mean (SD) population pharmacokinetic derived AUC12h and C0h in the pooled Phase III trials, DUET-1 and DUET-2, was 5506 (4710) ng.h/mL and 393 (391) ng/mL, respectively (N = 575)].

Therefore, to minimize underexposure to TMC125 and to provide exposures comparable to those observed in adults, 5.2 mg/kg b.i.d. is the proposed dose for HIV-1 infected children and adolescents between the ages of 6 and 17 years, inclusive.

2.2.2.3. Safety results

Safety analysis from Stage 1 and 2 showed that TMC125 at 4 mg/kg and 5.2 mg/kg b.i.d. was generally safe and well tolerated. Overall, 14 subjects (66.7%) and 9 subjects (42.9%) reported at least 1 AE in Stage 1 and 2, respectively. The most common AEs were headache and rhinitis. The majority of events were grade 1 or 2. One subject in prematurely discontinued the trial due to grade 3 increased blood creatinine in the predose sample on Day 1 that was considered not related to TMC125. One subject had an asymptomatic grade 4 increased triglycerides. No other grade 3 or 4 AEs were reported during the course of the trial.

2.3. MAH's conclusion

A weight adjusted dose of etravirine based on 5.2 mg/kg b.i.d. was selected for treatment experienced paediatric subjects aged 6 to 17 years based on the pharmacokinetics of etravirine in adults from the DUET trials and the overall safety of etravirine in Stage II of TMC125-C126 trial.

Further development is currently ongoing in trial TMC125-TiDP35-C213 where the safety, tolerability, antiviral activity and population pharmacokinetics of etravirine are investigated in children and adolescents aged 6-17 years.

TMC125-TiDP35-C213

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. 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. Safety will be monitored throughout the study. Additional assessment includes changes in the HIV-1 genotype, drug susceptibility, and the

population pharmacokinetics of TMC125. The primary analysis will be performed when all enrolled subjects have completed the 24 weeks assessment or have discontinued earlier.

It is anticipated that an extension application to support a pediatric indication will be submitted in **4Q2011**. The timelines are driven by the ongoing Phase II clinical trial TMC125-TiDP35-C213.

Line-listing of clinical studies in paediatric patients

Study title	Study number	Date of completion	Date of submission of final study report
A Phase I, open-label trial to investigate pharmacokinetics, safety and tolerability of TMC125 at steadystate in treatment-experienced HIV-infected children.	TMC125-C126	27 Feb 2008	21 January 2010
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.	TMC125-TiDP35-C213	Ongoing	
A Phase II, open-label trial to evaluate the safety, tolerability, pharmacokinetics and antiviral activity of TMC125 in antiretroviral experienced HIV-1 infected infants and children aged >2 months to < 6 years.	TMC125-TiDP35-C234	Planned	

3. Rapporteur's Overall Conclusion AND RECOMMENDATION

The MAH submitted the final report for TMC125-C126, a Phase I, open-label trial to investigate the pharmacokinetics, safety and tolerability of TMC125 at steady state in treatment-experienced HIV-infected children.

A weight adjusted dose of 5.2 mg/kg b.i.d. was selected for etravrine treatment experienced paediatric subjects aged 6 to 17 years, based on the comparable exposure achieved with this dose and those seen in adults (DUET trials) and its overall safety in Stage II of TMC125-C126 trial.

This dose has been already mentioned in the Pediatric Investigation Plan for etravirine and is endorsed by the Rapporteur.

This study is part of the clinical development program for Intelence in paediatric patients. A full package, including study TMC125-C126 is anticipated to be submitted by 4Q2011. A full benefit/risk assessment will be made in the frame of the upcoming procedure.

Recommendation

☒ **Fulfilled –**

No further action required, however further data are expected in the context of a type II variation anticipated to be submitted by 4Q2011.