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Trial record **1 of 1** for: TMC278-TIDP6-C215

Previous Study | Return to List | Next Study

# TMC278-TiDP6-C215: A Clinical Trial in Treatment Naive HIV-subjects Patients Comparing TMC278 to Efavirenz in Combination With 2 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

**This study has been completed.**

**Sponsor:**
Tibotec Pharmaceuticals, Ireland

**Information provided by (Responsible Party):**
Tibotec Pharmaceuticals, Ireland

**ClinicalTrials.gov Identifier:**
NCT00543725

First received: October 11, 2007
Last updated: March 3, 2016
Last verified: March 2016
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Results First Received: June 14, 2011

| | |
|---|---|
| **Study Type:** | Interventional |
| **Study Design:** | Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study;<br>Intervention Model: Parallel Assignment;<br>Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor);<br>Primary Purpose: Treatment |
| **Conditions:** | HIV Infections<br>HIV-1 |
| **Interventions:** | Drug: TMC278<br>Drug: efavirenz |

## Participant Flow

Hide Participant Flow

### Recruitment Details

| **Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations** |
|---|
| A phase III, randomized, double-blind trial of TMC278 25 mg q.d. versus efavirenz 600mg q.d. in combination with a background regimen containing 2 nucleoside/nucleotide reverse transcriptase inhibitors in antiretroviral-naïve HIV-1 infected subjects |

### Pre-Assignment Details

| **Significant events and approaches for the overall study following participant enrollment, but prior to group assignment** |
|---|
| 680 participants were randomized (340 in TMC 278 and 340 in efavirenz) but only 338 participants were treated with efavirenz (2 were randomized but not treated). |

### Reporting Groups

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

### Participant Flow: Overall Study

| | TMC278 | Efavirenz |
|---|---|---|
| STARTED | 340 | 338 |
| COMPLETED | 272 | 264 |
| NOT COMPLETED | 68 | 74 |
| Adverse Event | 18 | 27 |
| Sponsor's Decision | 0 | 1 |
| Subject Non-Compliant | 4 | 4 |
| Subject Ineligible To Continue The Trial | 2 | 0 |
| Subject Reached A Virologic Endpoint | 22 | 14 |
| Protocol Violation | 0 | 1 |
| Withdrawal by Subject | 4 | 13 |
| Lost to Follow-up | 15 | 11 |
| Not specified | 3 | 3 |

## Baseline Characteristics

Hide Baseline Characteristics

### Population Description

| Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate. |
|---|
| No text entered. |

### Reporting Groups

| | Description |
|---|---|
| TMC278 | 25 mg tablet once daily |
| Efavirenz | 600 mg once daily |
| Total | Total of all reporting groups |

### Baseline Measures

| | TMC278 | Efavirenz | Total |
|---|---|---|---|
| Number of Participants [units: participants] | 340 | 338 | 678 |
| Age [units: participants] | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 339 | 337 | 676 |
| >=65 years | 1 | 1 | 2 |
| Age [units: years] Mean (Standard Deviation) | 36.7 (9.39) | 36.4 (8.92) | 36.5 (9.15) |
| Gender [units: participants] | | | |
| Female | 90 | 94 | 184 |
| Male | 250 | 244 | 494 |

| Region Enroll [units: participants] | | | |
|---|---|---|---|
| Africa | 19 | 38 | 57 |
| Asia | 59 | 61 | 120 |
| Latin America | 90 | 85 | 175 |
| USA, Canada, Europe, Australia | 172 | 154 | 326 |

## Outcome Measures

Hide All Outcome Measures

1. Primary: Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 Copies Per mL) at Week 48 [ Time Frame: Week 48 ]

| | |
|---|---|
| **Measure Type** | Primary |
| **Measure Title** | Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 Copies Per mL) at Week 48 |
| **Measure Description** | Virological response is defined as confirmed plasma viral load less than (<) 50 human immunodeficiency virus-1 (HIV-1) (ribonucleic acid [RNA]) copies/milliliter (ml) at Week 48. The TLOVR algorithm was used to derive response. Response needed to be confirmed at 2 consecutive visits and participants who permanently discontinued were considered nonresponders after discontinuation. Resuppression after confirmed virologic failure was considered as failure. Virologic Failure includes participants who were rebounder (confirmed viral load >= 50 copies/ml after being responder) or who were never suppressed (no confirmed viral load <50 copies/ml). |
| **Time Frame** | Week 48 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 340 | 338 |
| **Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 Copies Per mL) at Week 48 [units: Participants]** | | |
| Responder | 291 | 276 |
| Virologic failure | 24 | 18 |
| Death | 1 | 3 |
| Discontinued due to AE | 8 | 21 |

| | | |
|---|---|---|
| **Discontinued due to other reason than AE** | **16** | **20** |

**Statistical Analysis 1 for Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 Copies Per mL) at Week 48**

| | |
|---|---|
| **Groups [1]** | All groups |
| **Non-Inferiority/Equivalence Test [2]** | Yes |
| **Method [3]** | Regression, Logistic |
| **P Value [4]** | <0.0001 |
| **Difference in proportion of response [5]** | 3.7 |
| **95% Confidence Interval** | -1.6 to 9.0 |

| | |
|---|---|
| **[1]** | Additional details about the analysis, such as null hypothesis and power calculation: |
| | Assuming a response rate of 75% at 48 weeks for both treatment groups, 340 subjects were needed per treatment (TMC278 or EFV) to establish non-inferiority of TMC278 versus EFV with a maximum allowable difference of 12% and a 1-sided significance level of 2.5%, to yield 95% power. |
| **[2]** | Details of power calculation, definition of non-inferiority margin, and other key parameters: |
| | If the lower limit of the 95% 2-sided confidence interval of the difference in proportions (TMC278 – EFV) exceeds -12%, non-inferiority of TMC278 versus EFV can be concluded. |
| **[3]** | Other relevant method information, such as adjustments or degrees of freedom: |
| | Logistic regression model included treatment arm and background NRTI regimen as factors, and baseline (log10) viral load as covariate. |
| **[4]** | Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance: |
| | Significance level was set at 2.5% (one-sided). No adjustment of p-value for multiple comparisons, since there was only single comparison for the primary endpoint. |
| **[5]** | Other relevant estimation information: |
| | Difference in proportion responders was estimated through the logistic regression model. |

2. Secondary: Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 48 [ Time Frame: Week 48 ]

| | |
|---|---|
| **Measure Type** | Secondary |
| **Measure Title** | Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 48 |
| **Measure Description** | The analysis is based on the last observed viral load (VL) data within the Week 48 window. Virologic response is defined as a VL<50 copies/mL (observed case). Missing VL was considered as non-response. Virologic Failure includes subjects who had VL>=50 copies/mL in the Wk 48 window, subjects who discontinued early due to lack or loss of efficacy, subjects who discontinued for reasons other than an adverse event, death or lack or loss of efficacy and at the time of discontinuation had a VL>=50 copies/mL and subjects who had a switch in background regimen that was not permitted by the protocol. |
| **Time Frame** | Week 48 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | **340** | **338** |
| **Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 48 [units: Participants]** | | |
| **Virologic Response (<50 copies/mL)** | **281** | **265** |
| **Virologic failure** | **41** | **38** |
| **No plasma viral load data in 48-week window** | **18** | **35** |

**Statistical Analysis 1 for Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 48**

| | |
|---|---|
| **Groups [1]** | All groups |
| **Non-Inferiority/Equivalence Test [2]** | Yes |
| **Method [3]** | Regression, Logistic |
| **P Value [4]** | <0.0001 |
| **Difference in proportion of response [5]** | 3.9 |
| **95% Confidence Interval** | -1.9 to 9.6 |

| | |
|---|---|
| **[1]** | Additional details about the analysis, such as null hypothesis and power calculation: |
| | No text entered. |
| **[2]** | Details of power calculation, definition of non-inferiority margin, and other key parameters: |
| | If the lower limit of the 95% 2-sided confidence interval of the difference in proportions (TMC278 – EFV) exceeds -12%, non-inferiority of TMC278 versus EFV can be concluded. |
| **[3]** | Other relevant method information, such as adjustments or degrees of freedom: |
| | Logistic regression model included treatment arm and background NRTI regimen as factors, and baseline (log10) viral load as covariate. |
| **[4]** | Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance: |
| | No text entered. |
| **[5]** | Other relevant estimation information: |
| | Difference in proportion responders was estimated through the logistic regression model. |

3. Secondary: Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 Copies Per mL) at Week 96 [ Time Frame: Week 96 ]

| | |
|---|---|
| **Measure Type** | Secondary |
| | Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 |

| | |
|---|---|
| **Measure Title** | Copies Per mL) at Week 96 |
| **Measure Description** | No text entered. |
| **Time Frame** | Week 96 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | **340** | **338** |
| **Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 Copies Per mL) at Week 96 [units: Participants]** | | |
| **Responder** | **269** | **258** |
| **Virologic failure** | **34** | **24** |
| **Death** | **1** | **3** |
| **Discontinued due to AE** | **16** | **23** |
| **Discontinued due to other reason than AE** | **20** | **30** |

**Statistical Analysis 1 for Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <50 Copies Per mL) at Week 96**

| | |
|---|---|
| **Groups [1]** | All groups |
| **Non-Inferiority/Equivalence Test [2]** | Yes |
| **Method [3]** | Regression, Logistic |
| **P Value [4]** | <0.0001 |
| **Difference in proportion of response [5]** | 2.4 |
| **95% Confidence Interval** | -3.6 to 8.4 |

| | |
|---|---|
| **[1]** | Additional details about the analysis, such as null hypothesis and power calculation: |
| | Assuming a response rate of 75% at 48 weeks for both treatment groups, 340 subjects were needed per treatment (TMC278 or EFV) to establish non-inferiority of TMC278 versus EFV with a maximum allowable difference of 12% and a 1-sided significance level of 2.5%, to yield 95% power. |
| **[2]** | Details of power calculation, definition of non-inferiority margin, and other key parameters: |
| | If the lower limit of the 95% 2-sided confidence interval of the difference in proportions (TMC278 – EFV) exceeds -12%, non- |

| | |
|---|---|
| | inferiority of TMC278 versus EFV can be concluded. |
| [3] | Other relevant method information, such as adjustments or degrees of freedom: |
| | Logistic regression model included treatment arm and background NRTI regimen as factors, and baseline (log10) viral load as covariate. |
| [4] | Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance: |
| | Significance level was set at 2.5% (one-sided). No adjustment of p-value for multiple comparisons, since there was only single comparison for the primary endpoint. |
| [5] | Other relevant estimation information: |
| | Difference in proportion responders was estimated through the logistic regression model. |

4. Secondary: Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 96 [ Time Frame: Week 96 ]

| | |
|---|---|
| **Measure Type** | Secondary |
| **Measure Title** | Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 96 |
| **Measure Description** | No text entered. |
| **Time Frame** | Week 96 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | **340** | **338** |
| **Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 96 [units: Participants]** | | |
| **Virologic response (<50 copies/mL)** | **259** | **254** |
| **Virologic failure** | **53** | **38** |
| **No plasma viral load data in 96-Week window** | **28** | **46** |

**Statistical Analysis 1 for Number of Participants With Virological Response (Intent-to-Treat - Snapshot, <50 Copies Per mL) at Week 96**

| | |
|---|---|
| **Groups [1]** | All groups |
| **Non-Inferiority/Equivalence Test [2]** | Yes |
| | |

| | |
|---|---|
| **Method** [3] | Regression, Logistic |
| **P Value** [4] | <0.0001 |
| **Difference in proportion of response** [5] | 0.7 |
| **95% Confidence Interval** | -5.6 to 7.0 |

| | |
|---|---|
| [1] | Additional details about the analysis, such as null hypothesis and power calculation: |
| | No text entered. |
| [2] | Details of power calculation, definition of non-inferiority margin, and other key parameters: |
| | If the lower limit of the 95% 2-sided confidence interval of the difference in proportions (TMC278 – EFV) exceeds -12%, non-inferiority of TMC278 versus EFV can be concluded. |
| [3] | Other relevant method information, such as adjustments or degrees of freedom: |
| | Logistic regression model included treatment arm and background NRTI regimen as factors, and baseline (log10) viral load as covariate. |
| [4] | Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance: |
| | No text entered. |
| [5] | Other relevant estimation information: |
| | Difference in proportion responders was estimated through the logistic regression model. |

5. Secondary: Number of Participants With Virological Response (Observed, <50 Copies/mL) at Last On-Treatment Visit (Post-Week 96). [ Time Frame: Variable, ranging from 3 months up to maximum 18 months for TMC278 and 12 months for Efavirenz ]

| | |
|---|---|
| **Measure Type** | Secondary |
| **Measure Title** | Number of Participants With Virological Response (Observed, <50 Copies/mL) at Last On-Treatment Visit (Post-Week 96). |
| **Measure Description** | Virological response is defined as (observed) plasma viral load less than 50 human immunodeficiency virus-type 1 (HIV-1) ribonucleic acid (RNA) copies per mL at the last on-treatment post-Week 96 visit. |
| **Time Frame** | Variable, ranging from 3 months up to maximum 18 months for TMC278 and 12 months for Efavirenz |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| Participants with at least 1 Post-Week 96 visit were included in the analysis. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | **269** | **257** |

| | | |
|---|---|---|
| **Number of Participants With Virological Response (Observed, <50 Copies/mL) at Last On-Treatment Visit (Post-Week 96).<br>[units: Participants]** | **260** | **246** |

**No statistical analysis provided for Number of Participants With Virological Response (Observed, <50 Copies/mL) at Last On-Treatment Visit (Post-Week 96).**

6. Secondary: Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 48 [ Time Frame: Week 48 ]

| | |
|---|---|
| **Measure Type** | Secondary |
| **Measure Title** | Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 48 |
| **Measure Description** | Virological response is defined as confirmed plasma viral load < 400 HIV-1 (RNA) copies/mL at Week 48. The TLOVR algorithm was used to derive response. Response needed to be confirmed at 2 consecutive visits and participants who permanently discontinued were considered nonresponders after discontinuation. Resuppression after confirmed virologic failure was considered as failure. Virologic Failure includes participants who were rebounder (confirmed viral load >= 400 copies/mL after being responder) or who were never suppressed (no confirmed viral load <400 copies/mL). |
| **Time Frame** | Week 48 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. |

**Reporting Groups**

| | **Description** |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | **TMC278** | **Efavirenz** |
|---|---|---|
| **Number of Participants Analyzed<br>[units: participants]** | **340** | **338** |
| **Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 48<br>[units: Participants]** | **300** | **286** |

**No statistical analysis provided for Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 48**

7. Secondary: Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 96 [ Time Frame: Week 96 ]

| | |
|---|---|
| **Measure Type** | Secondary |
| **Measure Title** | Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 96 |

| | |
|---|---|
| **Measure Description** | Virological response is defined as confirmed plasma viral load < 400 HIV-1 (RNA) copies/mL at Week 96. The TLOVR algorithm was used to derive response. Response needed to be confirmed at 2 consecutive visits and participants who permanently discontinued were considered nonresponders after discontinuation. Resuppression after confirmed virologic failure was considered as failure. Virologic Failure includes participants who were rebounder (confirmed viral load >= 400 copies/mL after being responder) or who were never suppressed (no confirmed viral load <400 copies/mL). |
| **Time Frame** | Week 96 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | **340** | **338** |
| **Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 96 [units: Participants]** | **283** | **270** |

**No statistical analysis provided for Number of Participants With Virological Response (Intent-to-Treat - Time to Loss of Virologic Response [TLOVR], <400 Copies Per mL) at Week 96**

8. Secondary: Mean Change From Baseline to Week 48 and Week 96 in Absolute and Relative CD4+ Cell Counts (Using Imputed Data) [ Time Frame: Baseline, Week 48, and Week 96 ]

| | |
|---|---|
| **Measure Type** | Secondary |
| **Measure Title** | Mean Change From Baseline to Week 48 and Week 96 in Absolute and Relative CD4+ Cell Counts (Using Imputed Data) |
| **Measure Description** | Change from baseline in CD4+ cell count was imputed in case of missing values: in case of premature discontinuation, data were imputed with the baseline value after discontinuation (i.e. change=0, Non-Completer [NC] = Failure); otherwise last observation carried forward was applied. |
| **Time Frame** | Baseline, Week 48, and Week 96 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | **339** | **338** |
| **Mean Change From Baseline to Week 48 and Week 96 in Absolute and Relative CD4+ Cell Counts (Using Imputed Data) [units: cells per microliter] Mean (95% Confidence Interval)** | | |
| **Absolute cell count, Week 48** | **188.6 (173.98 to 203.15)** | **170.7 (154.55 to 186.77)** |
| **Absolute cell count, Week 96** | **234.5 (217.40 to 251.55)** | **212.0 (193.70 to 230.34)** |
| **Relative cell count, Week 48** | **8.3 (7.68 to 8.85)** | **8.0 (7.39 to 8.60)** |
| **Relative cell count, Week 96** | **10.1 (9.35 to 10.75)** | **9.7 (8.95 to 10.40)** |

**No statistical analysis provided for Mean Change From Baseline to Week 48 and Week 96 in Absolute and Relative CD4+ Cell Counts (Using Imputed Data)**

9. Secondary: Number of Participants With Virologic Failure for the Resistance Determinations by Developing Mutations: First Available On-Treatment Genotypic Data After Failure [ Time Frame: Week 96 ]

| | |
|---|---|
| **Measure Type** | Secondary |
| **Measure Title** | Number of Participants With Virologic Failure for the Resistance Determinations by Developing Mutations: First Available On-Treatment Genotypic Data After Failure |
| **Measure Description** | Virologic failure for the resistance determinations was defined as lack of virologic response (never having had 2 consecutive plasma viral load <50 copies/mL) and plasma viral load increase of >=0.5 log 10 copies/mL above nadir (i.e., never suppressed), or confirmed loss of virologic response (2 consecutive plasma viral load >=50 copies/mL after having had 2 consecutive plasma viral load <50 copies/mL; i.e., rebounder), or discontinued with a last observed on-treatment plasma viral load >=50 copies/mL after having had 2 consecutive plasma viral load <50 copies/mL. For this study, treatment-emergent reverse transcriptase (RT) resistance associated mutations (RAMs) occurring in at least 2 virologic failures (for at least one treatment group) for the following lists are presented: i) Extended list of Non-nucleoside reverse transcriptase inhibitor (NNRTI RAMs) ii) IAS-USA list of Nucleoside/tide reverse transcriptase inhibitor (N[t]RTI RAMs). |
| **Time Frame** | Week 96 |
| **Safety Issue** | No |

**Population Description**

| |
|---|
| **Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.** |
| The Intent-to-Treat analysis set was considered the primary efficacy analysis set. Here "N" (Number of Participants Analyzed) signifies number of Participants who were evaluable (had data) for this outcome. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Measured Values**

| | TMC278 | Efavirenz |
|---|---|---|
| **Number of Participants Analyzed [units: participants]** | **34** | **24** |
| **Number of Participants With Virologic Failure for the Resistance Determinations by Developing Mutations: First Available On-Treatment Genotypic Data After Failure [units: Participants]** | | |
| **Treatment-emergent NNRTI RAM** | **17** | **11** |
| **E138K** | **13** | **1** |
| **H221Y** | **3** | **0** |
| **K101E** | **3** | **2** |
| **K103N** | **0** | **6** |
| **V90I** | **2** | **1** |
| **V106M** | **0** | **2** |
| **V189I** | **2** | **0** |
| **Y188C** | **0** | **2** |
| **Treatment-emergent N(t)RTI RAM** | **17** | **6** |
| **K65R** | **0** | **2** |
| **K219E** | **2** | **0** |
| **M184I** | **8** | **1** |
| **M184V** | **10** | **3** |

**No statistical analysis provided for Number of Participants With Virologic Failure for the Resistance Determinations by Developing Mutations: First Available On-Treatment Genotypic Data After Failure**

## Serious Adverse Events

Hide Serious Adverse Events

| | |
|---|---|
| **Time Frame** | Up to 164 weeks for participants in the TMC278 treatment group and up to 144 weeks for participants in the efavirenz treatment group. |
| **Additional Description** | Only participants who had at least one of the treatment-emergent adverse events (TEAEs) listed in the Other (non Serious) adverse event (AE) table are included in the total number of participants with Non-Serious AEs. |

**Reporting Groups**

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

**Serious Adverse Events**

| | TMC278 | Efavirenz |
|---|---|---|

| | | |
|---|---|---|
| **Total, serious adverse events** | | |
| **# participants affected / at risk** | **32/340 (9.41%)** | **31/338 (9.17%)** |
| **Blood and lymphatic system disorders** | | |
| **Anaemia** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **1/338 (0.30%)** |
| **Thrombocytopenia** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Pancytopenia** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **Neutropenia** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Cardiac disorders** | | |
| **Arteriospasm coronary** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Atrial fibrillation** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Eye disorders** | | |
| **Macular hole** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **Gastrointestinal disorders** | | |
| **Diarrhoea** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Inguinal hernia** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Intestinal obstruction** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Jejunitis** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Vomiting** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **1/338 (0.30%)** |
| **Abdominal pain** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **Pancreatitis** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **General disorders** | | |
| **Asthenia** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Non-cardiac chest pain** * 1 | | |
| **# participants affected / at risk** | **2/340 (0.59%)** | **2/338 (0.59%)** |
| **Pyrexia** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Hepatobiliary disorders** | | |
| **Cholecystitis acute** * 1 | | |

| | | |
|---|---|---|
| # participants affected / at risk | 2/340 (0.59%) | 0/338 (0.00%) |
| Cholelithiasis * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 1/338 (0.30%) |
| Hyperbilirubinaemia * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Hepatotoxicity * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Immune system disorders | | |
| Allergy to arthropod sting * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Drug hypersensitivity * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Food allergy * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Infections and infestations | | |
| Pneumonia * 1 | | |
| # participants affected / at risk | 2/340 (0.59%) | 1/338 (0.30%) |
| Bronchitis * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Bronchopneumonia * 1 | | |
| # participants affected / at risk | 2/340 (0.59%) | 0/338 (0.00%) |
| Furuncle * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Gastroenteritis viral * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Helicobacter gastritis * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Pulmonary tuberculosis * 1 | | |
| # participants affected / at risk | 2/340 (0.59%) | 0/338 (0.00%) |
| Cerebral toxoplasmosis * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Cyclosporidium infection * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Dysentery * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Encephalitis herpes * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Hepatitis c * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Herpes zoster * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 1/338 (0.30%) |
| Meningitis bacterial * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Pelvic inflammatory disease * 1 | | |

| | | |
|---|---|---|
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Respiratory tract infection * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Staphylococcal infection * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Arthritis gonococcal * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Bacterial sepsis * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Cellulitis * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Diarrhoea infectious * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| External ear cellulitis * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Gastroenteritis shigella * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Hepatitis b * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Secondary syphilis * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Injury, poisoning and procedural complications | | |
| Clavicle fracture * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Fall * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Humerus fracture * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Pelvic fracture * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Brain contusion * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Lumbar vertebral fracture * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Radius fracture * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Joint sprain * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Investigations | | |
| Brain scan abnormal * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Blood amylase increased * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Lipase increased * 1 | | |

| | | |
|---|---|---|
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| **Metabolism and nutrition disorders** | | |
| Dehydration * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| **Musculoskeletal and connective tissue disorders** | | |
| Foot deformity * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| **Neoplasms benign, malignant and unspecified (incl cysts and polyps)** | | |
| Uterine leiomyoma * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 2/338 (0.59%) |
| Hodgkin's disease * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| **Nervous system disorders** | | |
| Cerebellar infarction * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Convulsion * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Dizziness * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Cerebrovascular accident * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Grand mal convulsion * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Haemorrhage intracranial * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| **Psychiatric disorders** | | |
| Depression * 1 | | |
| # participants affected / at risk | 2/340 (0.59%) | 0/338 (0.00%) |
| Suicide attempt * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| Acute psychosis * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Alcohol withdrawal syndrome * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| Psychotic disorder due to a general medical condition * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |
| **Renal and urinary disorders** | | |
| Renal failure acute * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 1/338 (0.30%) |
| Acute prerenal failure * 1 | | |
| # participants affected / at risk | 1/340 (0.29%) | 0/338 (0.00%) |
| **Reproductive system and breast disorders** | | |
| Ovarian cyst * 1 | | |
| # participants affected / at risk | 0/340 (0.00%) | 1/338 (0.30%) |

| | | |
|---|---|---|
| **Respiratory, thoracic and mediastinal disorders** | | |
| **Pneumothorax** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Asthma** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **Respiratory failure** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **Skin and subcutaneous tissue disorders** | | |
| **Pruritus generalised** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |
| **Palmar-plantar erythrodysaesthesia syndrome** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **Rash** * 1 | | |
| **# participants affected / at risk** | **0/340 (0.00%)** | **1/338 (0.30%)** |
| **Dermal cyst** * 1 | | |
| **# participants affected / at risk** | **1/340 (0.29%)** | **0/338 (0.00%)** |

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 11.0

## Other Adverse Events

Hide Other Adverse Events

| | |
|---|---|
| **Time Frame** | Up to 164 weeks for participants in the TMC278 treatment group and up to 144 weeks for participants in the efavirenz treatment group. |
| **Additional Description** | Only participants who had at least one of the treatment-emergent adverse events (TEAEs) listed in the Other (non Serious) adverse event (AE) table are included in the total number of participants with Non-Serious AEs. |

### Frequency Threshold

| | |
|---|---|
| **Threshold above which other adverse events are reported** | 5% |

### Reporting Groups

| | Description |
|---|---|
| **TMC278** | 25 mg tablet once daily |
| **Efavirenz** | 600 mg once daily |

### Other Adverse Events

| | TMC278 | Efavirenz |
|---|---|---|
| **Total, other (not including serious) adverse events** | | |
| **# participants affected / at risk** | **253/340 (74.41%)** | **259/338 (76.63%)** |
| **Gastrointestinal disorders** | | |
| **Nausea** * 1 | | |
| **# participants affected / at risk** | **57/340 (16.76%)** | **67/338 (19.82%)** |
| **Diarrhoea** * 1 | | |
| **# participants affected / at risk** | **49/340 (14.41%)** | **53/338 (15.68%)** |

| | | |
|---|---|---|
| Vomiting * 1 | | |
| # participants affected / at risk | 22/340 (6.47%) | 26/338 (7.69%) |
| General disorders | | |
| Fatigue * 1 | | |
| # participants affected / at risk | 20/340 (5.88%) | 29/338 (8.58%) |
| Pyrexia * 1 | | |
| # participants affected / at risk | 15/340 (4.41%) | 17/338 (5.03%) |
| Infections and infestations | | |
| Nasopharyngitis * 1 | | |
| # participants affected / at risk | 50/340 (14.71%) | 47/338 (13.91%) |
| Upper respiratory tract infection * 1 | | |
| # participants affected / at risk | 43/340 (12.65%) | 37/338 (10.95%) |
| Bronchitis * 1 | | |
| # participants affected / at risk | 31/340 (9.12%) | 6/338 (1.78%) |
| Influenza * 1 | | |
| # participants affected / at risk | 32/340 (9.41%) | 30/338 (8.88%) |
| Pharyngitis * 1 | | |
| # participants affected / at risk | 20/340 (5.88%) | 14/338 (4.14%) |
| Anogenital warts * 1 | | |
| # participants affected / at risk | 17/340 (5.00%) | 14/338 (4.14%) |
| Sinusitis * 1 | | |
| # participants affected / at risk | 17/340 (5.00%) | 19/338 (5.62%) |
| Musculoskeletal and connective tissue disorders | | |
| Back pain * 1 | | |
| # participants affected / at risk | 16/340 (4.71%) | 30/338 (8.88%) |
| Arthralgia * 1 | | |
| # participants affected / at risk | 10/340 (2.94%) | 17/338 (5.03%) |
| Nervous system disorders | | |
| Headache * 1 | | |
| # participants affected / at risk | 61/340 (17.94%) | 53/338 (15.68%) |
| Dizziness * 1 | | |
| # participants affected / at risk | 42/340 (12.35%) | 111/338 (32.84%) |
| Somnolence * 1 | | |
| # participants affected / at risk | 17/340 (5.00%) | 28/338 (8.28%) |
| Psychiatric disorders | | |
| Insomnia * 1 | | |
| # participants affected / at risk | 38/340 (11.18%) | 21/338 (6.21%) |
| Abnormal dreams * 1 | | |
| # participants affected / at risk | 19/340 (5.59%) | 26/338 (7.69%) |
| Depression * 1 | | |
| # participants affected / at risk | 24/340 (7.06%) | 19/338 (5.62%) |
| Respiratory, thoracic and mediastinal disorders | | |
| Cough * 1 | | |
| # participants affected / at risk | 33/340 (9.71%) | 15/338 (4.44%) |

| | | |
|---|---|---|
| **Pharyngolaryngeal pain** * 1 | | |
| **# participants affected / at risk** | **19/340 (5.59%)** | **6/338 (1.78%)** |
| **Skin and subcutaneous tissue disorders** | | |
| **Rash** * 1 | | |
| **# participants affected / at risk** | **15/340 (4.41%)** | **49/338 (14.50%)** |
| **Pruritus** * 1 | | |
| **# participants affected / at risk** | **15/340 (4.41%)** | **17/338 (5.03%)** |
| **Vascular disorders** | | |
| **Hypertension** * 1 | | |
| **# participants affected / at risk** | **23/340 (6.76%)** | **12/338 (3.55%)** |

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 11.0

## Limitations and Caveats

Hide Limitations and Caveats

| **Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data** |
|---|
| No text entered. |

## More Information

Hide More Information

**Certain Agreements:**

| |
|---|
| Principal Investigators are **NOT** employed by the organization sponsoring the study. |
| There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed. |
| The agreement is:<br>☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.<br>☑ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.<br>☐ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. |

**Results Point of Contact:**

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**Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):**

Rimsky L, Van Eygen V, Hoogstoel A, Stevens M, Boven K, Picchio G, Vingerhoets J. 96-Week resistance analyses of rilpivirine in treatment-naive, HIV-1-infected adults from the ECHO and THRIVE Phase III trials. Antivir Ther. 2013;18(8):967-77. doi: 10.3851/IMP2636. Epub 2013 May 28.

Nelson M, Amaya G, Clumeck N, Arns da Cunha C, Jayaweera D, Junod P, Li T, Tebas P, Stevens M, Buelens A, Vanveggel S, Boven K; ECHO

and THRIVE Study Groups. Efficacy and safety of rilpivirine in treatment-naive, HIV-1-infected patients with hepatitis B virus/hepatitis C virus coinfection enrolled in the Phase III randomized, double-blind ECHO and THRIVE trials. J Antimicrob Chemother. 2012 Aug;67(8):2020-8. doi: 10.1093/jac/dks130. Epub 2012 Apr 24.

Cohen CJ, Andrade-Villanueva J, Clotet B, Fourie J, Johnson MA, Ruxrungtham K, Wu H, Zorrilla C, Crauwels H, Rimsky LT, Vanveggel S, Boven K; THRIVE study group. Rilpivirine versus efavirenz with two background nucleoside or nucleotide reverse transcriptase inhibitors in treatment-naive adults infected with HIV-1 (THRIVE): a phase 3, randomised, non-inferiority trial. Lancet. 2011 Jul 16;378(9787):229-37. doi: 10.1016/S0140-6736(11)60983-5.

| | |
|---|---|
| Responsible Party: | Tibotec Pharmaceuticals, Ireland |
| ClinicalTrials.gov Identifier: | NCT00543725 History of Changes |
| Obsolete Identifiers: | NCT00614692 |
| Other Study ID Numbers: | CR002704<br>**TMC278-TIDP6-C215** ( Other Identifier: Tibotec Pharmaceuticals, Ireland ) |
| Study First Received: | October 11, 2007 |
| Results First Received: | June 14, 2011 |
| Last Updated: | March 3, 2016 |
| Health Authority: | United States: Food and Drug Administration<br>Ireland: Irish Agriculture and Food Development Authority<br>Canada: Health Canada<br>China: Food and Drug Administration<br>Great Britain: Medicines and Healthcare Products Regulatory Agency<br>United States: Federal Government<br>Great Britain: Research Ethics Committee |

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Information in this posting shall not be considered to be a claim for any marketed Product. Some information in this posting may differ from the approved labeling for the Product. Please refer to the full prescribing information for indications and proper use of the product.