**Relative bioavailability of a concept paediatric formulation of TMC278, an investigational NNRTI**

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**Introduction**

- TMC278 (Figure 1) is a next-generation NNRTI that has demonstrated sustained efficacy and good tolerability in treatment-naive, HIV-infected adults over 120 weeks in a Phase II trial.
- TMC278 is currently being evaluated in two Phase IIb trials in adults in a tablet formulation or in a dose of 25 mg pg, in combination with a backbone of two NRTIs.
- Available treatment options for HIV-infected children are limited compared with the broad range of effective therapies developed for HIV-infected adults.

**Methods**

**Study design**

- Phases I, IIa, and randomised, three-way crossover in 12 healthy HIV-negative adults (n=2 in each group of 6, according to a Williams design) (Table 1).
- Participants received a single, oral 25 mg dose of TMC278 under fed or fasted conditions in the following dose forms:
  - Parenteral formulation: within 10 minutes of completion of a standardised breakfast (Treatment A).
  - Parenteral granule formulation after at least a 10-hour overnight fast (Treatment B).
  - Tablet (Phase II formulation used in ECHO [granules, fasted conditions] and Treatment C (tablet, fed conditions)).
- The tablet and granules were administered together with approximately 240 mL of water; the granules were dispersed in the water before intake, and the glass rinsed out after each use.
- There was a washout period of at least 14 days between two intakes of TMC278 (Table 2).
- The study protocol was reviewed and approved by the appropriate institutional ethics committee and health authority, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

**Volunteer disposition and baseline characteristics**

- Eleven of the volunteers completed the study and one was withdrawn after Session 1. Treatment B non-compliance with the study protocol.
- Baseline demographics are shown in Table 2.

**PK and statistical analysis**

- PK parameters were calculated using non-compartmental analysis.
- The primary PK parameters for the statistical analyses were maximum plasma concentration (C_{max}) and time to reach the maximum concentration (t_{max}).
- Plasma concentrations were quantifiable from 0.5 hours post-dose for the granule formulation administered in fasted conditions compared with intake with a meal. It will be recommended to administer the granules without food intake in the fasting state compared with intake with a meal. It will be recommended to administer the granules without food intake in the fasting state compared with intake with a meal. It will be recommended to administer the granules without food intake in the fasting state compared with intake with a meal. It will be recommended to administer the granules without food intake in the fasting state compared with intake with a meal.

**Results**

**Table 2. Baseline demographics.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>28 (21–40)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 1 (8.3)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian 9 (75.0)</td>
</tr>
<tr>
<td>Gender</td>
<td>Caucasian 9 (75.0)</td>
</tr>
<tr>
<td>Height,* cm</td>
<td>182.3 (165–192)</td>
</tr>
<tr>
<td>Weight,* kg</td>
<td>80.7 (68–98)</td>
</tr>
<tr>
<td>BMI,* kg/m²</td>
<td>25.1 (21.3–29.8)</td>
</tr>
</tbody>
</table>

**PK analyses**

- **Phase I** plasma concentration-time profiles and PK parameters:
  - Evaluation of the PK parameters for the granule formulation administered in fasted and fed conditions compared with intake with a meal.
- Plasma concentration-time profile was higher after administration of the granule formulation compared with the fed tablet formulation (Figure 2).

**Conclusions**

- The exposure (AUC_{last}) to TMC278 was 24% higher when administered as granule compared with the tablet, both taken with a meal.
- The exposure for the granule formulation administered in fasted conditions was comparable with that of the tablet formulation taken with a meal.
- The bioavailability of TMC278 administered as granules is affected by food intake, with a 28–30% lower exposure (AUC_{last}) when the granules were administered in the fasting state compared with intake with a meal. It will be recommended to take the granules with a meal.
- All treatments were generally well tolerated. No new safety signals for AEs, laboratory parameters, vital signs or ECGs were observed.
- The TMC278 granule formulation showed good oral bioavailability and palatability, and will be further developed for use in paediatric trials.

**Acknowledgements and disclosures**

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- We would like to express gratitude to...

References


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