The objective of the current study was to describe differences in populations of a pooled analysis between those who received shorter DoRx versus longer therapy in a phase 3 cIAI study. It was hypothesized that patients with longer courses of antibiotic therapy for cIAI are more complex patient population, presenting with more comorbidities, for whom clinicians choose to give longer antibiotic DoRx.

Methods

Post-hoc analysis from IGNITE1: The micro-ITT population was used to describe patient characteristics based on DoRx in a pooled group (ERV and ETP) at the primary test of cure visit.

IGNITE1 Study Design:

Stratification based upon site of infection (complicated appendicitis versus other)

Key Inclusion Criteria

Age ≥ 18 y
Hospitalized for confirmed cIAI (criteria from FDA guidance)
with adequate source drainage either planned or performed within 24 h
Evidence of a systemic inflammatory response

Length of antibiotic therapy was at the discretion of the investigator up to 14 d

Data Analysis

Univariate analyses (multi-group chi-square and Fisher exact test) were used to evaluate differences in baseline characteristics among 3 groups (≤ 5 d, 5.5-8 d, 8-14 d) based on DoRx

Logistic regression using a cumulative logit model was used to identify those factors associated independently with DoRx

Introduction

The appropriate duration of antimicrobial therapy (DoRx) for cIAI remains uncertain. A recent publication demonstrated that patients with cIAI who had undergone an adequate source-control procedure were less likely to have a diagnosis of complicated appendicitis, and were more likely to have an open procedure as compared to those receiving shorter DoRx (Table). Overall average DoRx was 7.1 d, and for each of the groups were ≤ 5 d, 5.5-8 d, and >8 d.

Conclusions

In this Phase 3 study where investigators were able to choose DoRx for up to 14 d, longer therapy was independently associated with concomitant bacteremia, a higher APACHE II score, a non-appendicitis diagnosis, and an open source control procedure. It is logical that bacteremic patients receive longer DoRx, although gram-negative bacteremia with adequate source control ordinarily does not require DoRx > 7 d. Clinical outcomes at TOC did not differ based on DoRx in the ME and CE populations, although a difference was observed in the micro-ITT population. The micro-ITT population may be suboptimal to evaluate outcomes based on DoRx, because the group with the shortest DoRx includes several patients for whom DoRx was not investigator-determined.

Results

Three groups were categorized based on DoRx ≤ 5 d, 5.5-8 d, and >8 d.

Mean overall DoRx was 7.1 d and 4.2 d, 6.8 d, and 11.2 d in the groups, respectively.

By univariate analysis (c2 or Fisher Exact Test), higher APACHE II score, age, complicated appendicitis (compared to other diagnoses), and open source control treatment (compared with other interventions) differed significantly among groups (Table 2).

Bacteremia trended to significance (p = 0.06). By multivariable logistic regression, higher APACHE II score, bacteremia, non-appendicitis diagnosis, and open surgery were independently associated with prolonged DoRx (Tables 2 and 3).

Clinical outcomes in the ME and CE populations were not associated with DoRx (Table 4).

Univariate and multivariate analyses in the ME and CE TOC populations were similar (data not shown) to those reported herein for the micro-ITT TOC population.

Table 1. Analysis Populations Definition

Table 2. Univariate Analysis of Patient Characteristics Based on DoRx in the micro-ITT Population

Table 3. Logistic Regression of Parameters Associated with DoRx in the micro-ITT Population

Table 4. Logistic Regression of Parameters Associated with DoRx in the micro-ITT Population (Removing Age-Reduced Model)

Table 5. Clinical Outcomes at the TOC Visit in the Different Populations

Holly L. Hoffman-Roberts1, Patrick J. Scoble1, Andrew J. Marsh1, Philip S. Barie2, Patrick T. Horn1

A pooled, post-hoc evaluation of the length of antibiotics therapy from IGNITE1: A phase 3 study of eravapen (ERV) and erapenem (ETP) for complicated intra-abdominal infections (cIAI)

Introduction

Background: The clinical decision to treat cIAI in patients with other antibiotic source-controlling variables occurs soon after the onset of antibiotic therapy. It is desirable to determine the length of therapy (> 5 d)

Methods: Patients with documented cIAI were randomized (1:1) to either ERV 1 mg/kg IV q12h or ETP 1 g IV QD. DoRx was up to 14 d at the clinician’s discretion. The micro-ITT population was used to describe patient characteristics based on DoRx in a pooled group (ERV and ETP) at the primary test of cure visit.

Results

Clinical outcome at the test of cure (TOC) visit, ~28 d after randomization, was the primary efficacy endpoint in the trial. The micro-ITT population was used to describe patient demographics and outcomes by duration of therapy (DoRx). Patients with documented cIAI were randomized (1:1) to either ERV 1 mg/kg IV q12h or ETP 1 g IV QD. DoRx was up to 14 d at the clinician’s discretion.

Clinical success was defined as no clinical signs and symptoms of disease, improvement in signs and symptoms of disease, or no change in signs and symptoms of disease in patients with documented cIAI who had undergone an adequate source-control procedure. The test of cure visit was defined as the first follow-up visit (28 d after randomization) when the clinician made the determination of clinical success.

Clinical outcomes in the ME and CE populations were not associated with DoRx.

Disclosures

This study was supported by Tetraphase Pharmaceuticals, Inc.

References