Novel Long-Acting Ropeginterferon Alfa-2b: Pharmacokinetics, Pharmacodynamics, and Safety in a Phase I Clinical Trial

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Abstract

AIM Ropeginterferon alfa-2b is a new site-specific conjugated 40 kDa branched polyethylene-glycol recombinant interferon (IFN). The aim of the study was to determine its safety, pharmacokinetics (PK) and pharmacodynamic (PD). METHODS Ropeginterferon alfa-2b was evaluated first in human in 48 healthy male volunteers after a single dose subcutaneous injection by either 24, 48, 90, 180, 225, 270mcg of the product or 180mcg of marketed pegylated (peg)-IFN alfa-2a. Within each dosing group, 6 subjects received ropeginterferon alfa-2b and 2 subjects received peg-IFN alfa-2a. RESULTS Dose-related increases in ropeginterferon alfa-2b PK parameters (Cmax, AUC, and AUC0-t) were observed over the dose range 24 to 270mcg. The geometric mean values for these PK parameters of ropeginterferon alfa-2b were higher than that of peg-IFN alfa-2a at the 180mcg dose level of 176%, 166%, and 182%, respectively. Mean PD parameters (Emax, Tmax, and AUC0-t) for ropeginterferon alfa-2b increased with dose for both biomarkers neopterin and 2', 5'-OAS. Ropeginterferon alfa-2b has similar PD profiles as peg-IFN alfa-2a. The treatment related adverse events are similar between the two study drugs, but the overall incidence was numerically lower for ropeginterferon alfa-2b (83%) than peg-IFN alfa-2a (100%) at the 180mcg dose level. CONCLUSIONS Single subcutaneous dose of Ropeginterferon alfa-2b of up to 270mcg is safe and well tolerated. It displays dose related increase in PK and PD parameters, potentially less frequent injection, and better safety profiles. Ropeginterferon alfa-2b is being developed for diseases in which previous peg-IFN use has been limited by side effects.

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a Phase I Clinical Trial

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Ropeginterferon alfa-2b Phase I Study in Healthy Subjects

Keywords: interferon; pegylated interferon; phase 1; first in human

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Data availability statement

The data that support the findings of this study are available on request to the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Authorship statement

CLT proposed the concept for study and contributed to the design of the study. JF participated in design of the study, preparation of the protocol, case report form, acted as the medical monitor, review of data/analyses, internal and external presentation and preparation of clinical study report. YWH, CWT and AQ contributed to the writing of the manuscript and interpretation of the data. RL was principal investigator to conduct study and contributed to acquisition, analysis and interpretation of data. All authors reviewed and approved the final manuscript.

Conflict of interest disclosure

Jane Fang served as a clinical research consultant for PharmaEssentia Corp. in this study. The other authors have no conflicts of interest to declare.

Ethics approval statement

The study was conducted in accordance with the provisions of the Declaration of Helsinki and its amendments, US Food and Drug Administration (FDA) guidance, and principles of Good Clinical Practice (GCP) from the International Conference on Harmonization (ICH) guidelines. The protocol and informed consent form were reviewed and approved by an Institutional Review Board (IRB) prior to the screening or enrollment of any study participant.

Patient consent statement

The purpose of the study was explained to the patients before they provided their written informed consent. Patients were provided with copies of their signed informed consent forms. At the study center, the clinical staff was available to patients before they entered the study and throughout their participation in the study to answer questions about the study. Patients were informed about any new development during the study that might have influenced their continued participation in the study.

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Not applicable

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Clinical Trial Registration

This study was submitted to US FDA for IND (IND number: 105653) but not registered in ClinicalTrial.gov.

What is already known about this subject?

The marketed pegylated interferons have limited clinical use due to their side effects, which might also limit the optimal dose for better efficacy.

Pegylated interferons have potential roles in unmet medical needs and in broad therapeutic areas.

What this study adds?

Ropeginterferon alfa-2b is a novel pegylated interferon with superior pharmacokinetic parameters than the marketed pegylated interferon product, allowing biweekly injection.

Ropeginterferon alfa-2b has better safety profiles than the marketed pegylated interferon product.

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Fig. 1.

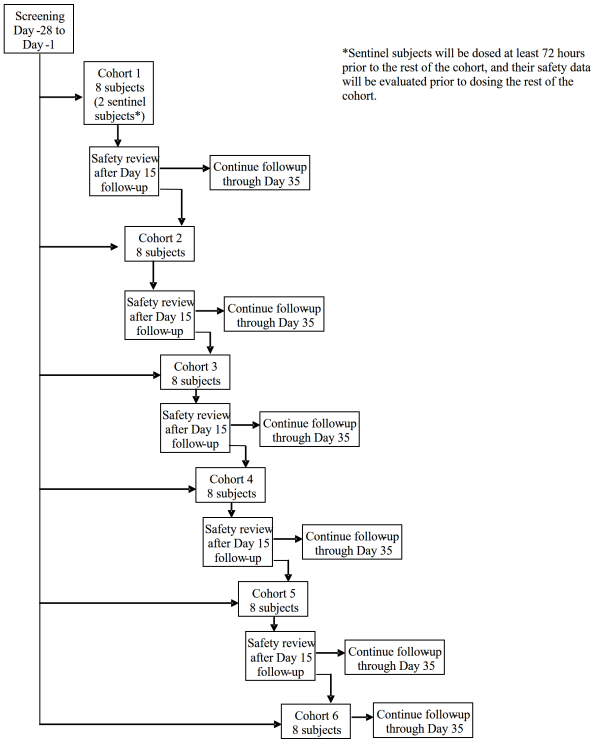

Fig. 2.