

P06.0502L

Universiteit Maastricht

Centrale Commissie Mensgebonden Onderzoek (CCMO)
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Maastricht
25/05/2006

Faculteit der Geneeskunde

Pulmonologie

Geachte heer/mevrouw,

Op 13 april 2006, hebben we een negatief advies ontvangen van de lokale Medisch Ethische Commissie van het Academisch Ziekenhuis Maastricht, voor het projectvoorstel getiteld: "A phase II, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, and pharmacokinetics of SUN11031 administered subcutaneously for 14 days in patients having cachexia associated with COPD".

Aangezien we geen gelegenheid hebben gekregen voor een weerwoord, willen we graag in administratief beroep gaan tegen dit advies, aangezien we van mening zijn dat de genoemde kritiekpunten goed te weerleggen zijn.

Bijgevoegd ontvangt u een puntsgewijze reactie op het negatieve advies. Graag vernemen we van u welke andere documenten u nog nodig heeft en of u deze direct via ons of via de lokale MEC van het AZM dient te ontvangen.

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Hoogachtend,

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c.c. Medisch Ethische Commissie
PO Box 5800
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CCMO ingekomen post	
Datum	10 ME 2006
Nummer	IN 06.1660
Aan	5.1.2.e
CC	
Scan	(ja) Nee

Bijlage: Respons op het negatieve advies



May 19, 2006

Notice of Appeal

MEC 06-1-042.25.1.2.e

Direct No: 043-3876009

Centrale Commissie Mensgebonden Onderzoek (CCMO)

P.O. Box 16302

2500 BH The Hague

Netherlands

Dear Sir or Madam,

Sponsor: Daiichi Asubio Pharmaceuticals, Inc.

Subject: Request for Appeal

Product Name: Synthetic Human Ghrelin

Protocol Number: ASBI 302

Protocol Title: A Phase II, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Tolerability and Pharmacokinetics of SUN 11031 Administered Subcutaneously for 14 days in Patients having Cachexia associated with COPD

In response to a letter from the Ethical Committee, University Hospital, Maastricht, dated April 13, 2006 in which the Medical Ethical Board issued a negative advice with regard to the study proposal listed above, we submit the following request for appeal.

We respectfully request that the Central Committee review our responses to the concerns noted in the letter with regard to this study to be conducted at the Asthma Center Hornerheide, Clinical Research Unit in Horne, Netherlands. Issues are presented in **bold font** and responses follow in normal text.

- 1) **"It is the Board's opinion that conducting the Phase 2 study before the Phase 1 study for subcutaneous administration is completed and its results are made available would be an irresponsible decision."**

The Phase 1 study ASBI 301, has fully enrolled and all dosing has been completed. All follow-up visits will be completed before the end of the month. We expect that final data will be available to share with you by late July. During the conduct of this study, we evaluated safety data at the completion of each dosing cohort before moving to the next dose. No serious adverse events or discontinuations due to adverse events have been reported.

The highest dose to be administered in the ASBI 302 study conducted at the Asthma Center Hornerheide, Clinical Research Unit, will not exceed the highest dose used in the 301 study.

2) "Uncertainties and estimated risks for the patients are currently too high and subject safety is insufficiently guaranteed"

We respectfully refer you to the Investigator's Brochure (Feb. 7, 2006, vers. #4) submitted with the filing. Based on publications available as of May, 2005, approximately 350 subjects have received varying dosages of ghrelin by bolus, prolonged infusion or subcutaneous injection. Administration regimens have been qd or bid for as little as 1 day through as long as 3 weeks. Adverse reactions reported have been mild in nature.

As patients in the ASBI 302 study will be housed and monitored on a 24-hour basis, we are prepared to address any safety event that may occur during the course of the study.

3) "... the Board deems the burden for the patients too high. ... patients will be subjected to many examinations....., the interests for the subjects and other current or future patients [as] unreasonably disproportional to the inconveniences and risks for the subjects."

The study protocol as proposed is embedded in an on-going COPD rehabilitation program at the hospital that uses cachexia as one of its selection criteria. Patients already remain in the center 5 days a week for 8 weeks and more than 300 patients a year are entered into this setting without experiencing the setting or procedures as a problem. Several of the tests required by the ASBI 302 protocol, which runs for only 2 weeks of the 8 week rehabilitation center study, are already included in the rehabilitation program and will NOT be duplicated. Screening period testing is addressed in the existing assessment by the rehabilitation center and follow-up period tests are partially covered by the outcomes also measured in the program. Days -13, 0, 1, 7 and 14 involve additional tests and blood sampling but ALL of these tests are performed within the context of the rehabilitation period. During the treatment period (Day 1-14), patients are required to stay in the center for 2 weekends. Patient's partners are invited to stay with them and recreational activities are planned for those weekends.

- 4) "It was also noted that the sponsor appears to have full access to all documents, including the medical files, without ensuring anonymity, which is not acceptable"

As noted in the protocol, we will ensure that patient confidentiality is upheld to the ICH guidelines and all other appropriate country regulations. If you have noted any inconsistent or contradictory text regarding patient confidentiality in our submission documents, we would be grateful for you to point this out so we can amend it accordingly.

We hope that our answers are sufficient to address your concerns and that you will allow the ASBI 302 study to proceed. If, however, these are not sufficient, then we respectfully request that you allow us more time to submit the final data from the ASBI 301 study before you issue your decision. Our database lock is scheduled for July 19, 2006 and we can provide information for you by the end of July.

We have copied [5.1.2.e] from the Medical Ethical Committee at the Clinical Trial Center in Maastricht on our response as a courtesy. We look forward to your review and timely response. Thank you very much for your consideration and please do not hesitate to contact the undersigned.

Sinc

[5.1.2.e]

University Hospital Maastricht
Department of Respiratory Medicine