Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer HealthCare

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer Healthcare AG	
Study Number:	BAY 86-5037/14853	NCT01092858
Study Phase:	IV Interventional	
Official Study Title:	Effect of exercise alone or in combination with testosterone replacement on muscle strength and quality of life in older men with low testosterone concentrations: a randomized double-blind, placebo controlled study	
Therapeutic Area:	Men' s Health	
Test Product		
Name of Test Product:	Testosterone undecanoate (NEBIDO, BAY 86-5037)	
Name of Active Ingredient:	Testosterone undecanoate	
Dose and Mode of Administration:	1000 mg (4 mL); intramuscular (IM) injection	
Reference Therapy/Placebo		
Reference Therapy:	matching placebo	
Dose and Mode of Administration:	not applicable; IM injection	
Duration of Treatment:	54 weeks	
Studied period:	Date of first subjects' first visit:	21 SEP 2010
	Date of last subjects' last visit:	06 JUL 2011
Premature Study Suspension / Termination:	The study was terminated due to low rate of eligible patients.	
Substantial Study Protocol Amendments:	The substantial modifications (ie, not administrative or editorial) resulting from Amendment 1, dated 28 JUN 2010, are as follows: • The inclusion criterion of symptomatic hypogonadism was	

	modified to better characterize hypogonadism • Withdrawal criterion regarding prostate safety was amended • The screening period was changed to comprise 2 visits, Visit 1.1 (to be conducted at -4 to -2 weeks) and Visit 1.2 (to be conducted no earlier than 24 hours after Visit 1.1 and no later than 2 weeks before Visit 2). The substantial modifications resulting from Amendment 2, dated 22 MAR 2011, are as follows: • The definition of the per protocol set was revised to add the requirement of adhering to the training plan • The procedure regarding Chip Cards was modified because due to the complex training program, the training at med.cologne could not be fully recorded on Chip Cards, as initially planned.
Study Centre(s):	1 study center in Germany randomized subjects
Methodology:	Eligible subjects were randomized to receive an IM injection of Nebido or placebo at Weeks 0, 6, 18, 30, and 42. No treatment was given at the final study visit at Week 54. Throughout the study, subjects participated in a protocol-prescribed training program that comprised both strength and endurance training. Subjects were evaluated at baseline, week 6 and every 12 weeks thereafter. Assessments included strength tests, endurance tests, vital signs, measurements of waist circumference, prostate examinations, adverse events (AEs), concomitant medications, and laboratory sampling (safety parameters, hormone levels, and metabolic biomarkers). The subjective well-being of the subjects was assessed by the AMS, SF-36, and FINGER questionnaires.
Indication/ Main Inclusion Criteria:	Male hypogonadism / Men aged 60 years and older (>/=60yrs), untrained. Symptomatic hypogonadism as defined by serum testosterone level below 12 nmol/L (two tests taken on two different days, measurement 7.00-11.00), symptoms of testosterone deficiency recorded in the medical history at screening and total Aging Males Symptoms Score (AMS) above 36.
Study Objectives:	<u>Primary:</u> The primary objective was to assess the additional effect of testosterone replacement therapy (TRT) in hypogonadal men on dynamic maximum strength (one repetition maximum [1-RM]) of the upper and lower extremities. <u>Secondary:</u> The secondary objectives were to assess the additional effect of TRT in hypogonadal men on further muscle parameters, endurance, cardiovascular parameters and quality of life (QoL).
Evaluation Criteria:	<u>Efficacy (Primary):</u> The primary efficacy variable was the change from baseline in dynamic maximum strength (one repetition maximum [1-RM]) of the upper and lower extremitiy (chest press, leg press) after 54 weeks of

	Nebido compared to placebo. Efficacy (Secondary): The AMS rating scale was to be used to assess symptoms of hypogonadism and to evaluate the change in severity of symptoms. The health related QoL of the subjects was also assessed by the SF-36 and FINGER questionnaires. The following assessments were also done: isometric maximum strength, grip strength, chair-rising test, arm-curl test, bicycle stress test with spirometry, pulse wave velocity, aortal augmentation index and interventricular septal thickness (Echocardiography). Safety: Safety assessments included vital signs, AEs, SAEs, Adverse events of special safety interest (Pulmonary oily microembolism, unexpected adverse drug reactions), pregnancies, laboratory parameters: hematology (hemoglobin, hematocrit), blood chemistry (lipds and liver function tests), Prostate specific antigen (PSA), breast and prostate (DRE) examinations.
Statistical Methods:	Efficacy : Because of the small sample size of this terminated study (n=4), no statistical analyses were performed.
Number of Subjects:	60 subjects in total were planned (30 per treatment group). Four subjects were treated; 3 subjects received Nebido and 1 subject received placebo.

Study Results
Results Summary — Subject Disposition and Baseline
Four subjects were randomized and treated; 3 subjects were treated with Nebido and 1 subject was treated with placebo. All 4 subjects prematurely discontinued the study; the 3 subjects treated with Nebido prematurely discontinued because the study was terminated early and the subject treated with placebo discontinued due to a prespecified withdrawal criterion (PSA level increase > / = 1.0 ng/ml above the baseline PSA, if baseline PSA was </= 2.0ng/ml).
Results Summary — Efficacy
No inferential efficacy analyses were conducted and no summary statistics for the efficacy variables were prepared.
Results Summary — Safety
No subject completed study treatment. Of the 3 subjects who received Nebido, one subject

received 4 injections, 1 subject received 3 injections, and one subject received 2 injections. The subject who received placebo received 3 injections.

One subject in the Nebido group experienced an AE, one subject in the Placebo group experienced an SAE, both of which were treatment-emergent, moderate in intensity, not considered related to study drug, and were in the system organ class Infections and infestations.

One subject (Nebido) came down with influenza (reported as “flue”), which was considered / classified not to be serious. The subject was treated with 100 mg acetyl salicylic acid as needed, and recovered after 19 days.

One subject (placebo) experienced a urinary tract infection. The event was considered serious because it resulted in hospitalization. The subject was treated and released from the hospital within 3 days. (The subject was subsequently withdrawn from the study due to a prespecified withdrawal criterion.)

Conclusion(s)

Due to the small number of subjects, no definitive conclusions can be drawn from this study regarding the efficacy or safety of Nebido.

Publication(s):	none
Date Created or Date Last Updated:	20 JUN 2012

Investigational Site List

Marketing Authorization Holder in Germany	
Name	Jenapharm GmbH & Co. KG
Postal Address	Otto-Schott-Straße 15 D-07745 Jena Germany
Sponsor in Germany (if applicable)	
Legal Entity Name	Bayer HealthCare AG
Postal Address	Building K56 D-51368 Leverkusen Germany

List of Investigational Sites

No	Investigator Name	Facility Name	Street	ZIP Code	City	Country
1	Fr. Prof. Dr. Ioanna Gouni-Berthold	Universitätsklinikum Köln	Klinik II und Poliklinik für Innere Medizin Kerpener Str. 62	50931	Köln	Germany