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:	12331	NCT00845338
Study Phase:	II	
Official Study Title:	A 4-week, open-label, multicenter, urodynamic pilot study to explore the efficacy, tolerability and safety of darifenacin (7.5 mg with up-titration to 15 mg) in patients with multiple sclerosis and neurogenic detrusor overactivity	
Therapeutic Area:	Urology	
Test Product		
Name of Test Product:	Darifenacin (Emselex, BAY79-4998)	
Name of Active Ingredient:	Darifenacin	
Dose and Mode of Administration:	Dose: 7.5 or 15.0 mg extended release tablets once daily (od) Mode of administration: oral	
Reference Therapy/Placebo		
Reference Therapy:	Not applicable	
Dose and Mode of Administration:	Not applicable	
Duration of Treatment:	28 days	
Studied period:	Date of first subjects' first visit:	16 FEB 2007
	Date of last subjects' last visit:	16 OCT 2007
Premature Study Suspension / Termination:	The study was prematurely terminated since the enrollment rate at most centers was unlikely to result in the recruitment of the planned sample size of 40 evaluable subjects that was needed to detect clinically meaningful changes in the volume of first contraction.	
Substantial Study Protocol Amendments:	Amendment no. 1 (dated 11 OCT 2006), specified the changes in the exclusion and trial termination criteria. In addition, the retaining of study documentation was also specified.	
Study Centre(s):	The study was planned at 6 centers and conducted at 5 centers in Germany.	
Methodology:	This was an open-label, single arm, multi-center pilot study with a planned 4-week treatment period. Subjects received daily doses of 7.5 mg darifenacin as extended release tablets for the first 2 weeks of the 4-week treatment period. Depending on the tolerability and safety of the initial dose regimen, subjects were up-titrated to 15 mg darifenacin per day until the end of the treatment period. Vital signs were assessed at all visits. Data related to primary efficacy variable (change from baseline in volume at first detrusor contraction) were planned to be assessed at week 4. Except for 7 day micturition diary evaluations at weeks 2 and 4, all other secondary efficacy variables	

	(detrusor pressure at first contraction, volume at first detectable leakage, volume at 10/20/30/40 cm H_2O detrusor pressure, subject compliance, and maximum cystometric bladder capacity) were planned to be assessed at week 4. Data related to the occurrence of adverse events and serious adverse events were collected at all visits after Visit 1 (screening).
Indication/ Main Inclusion Criteria:	Indication: Multiple sclerosis and neurogenic detrusor overactivity Main Inclusion Criteria: Subjects diagnosed with multiple sclerosis for at least 6 months and neurogenic detrusor overactivity without detrusor spincter dyssynergia.
Study Objectives:	Overall: To explore the effects of darifenacin in subjects with multiple sclerosis and neurogenic detrusor overactivity.
Evaluation Criteria:	Efficacy (Primary): The efficacy variable of primary interest was the change from baseline in volume at first detrusor contraction as determined by urodynamics. Efficacy (Secondary): The following urodynamic measurements served as secondary variables: • Detrusor pressure at first contraction • Volume at first detectable leakage • Volume at 10/20/30/40 cm H_2O detrusor pressure • Compliance • Maximum cystometric bladder capacity, which is defined as the volume at significant leakage (i.e., leakage that prevents further volume increase) or discomfort/pain. Furthermore, the change from baseline was planned to be calculated for parameters of a 7-day micturition diary. The diary would assess the number per day of: • Micturitions • Urgency episodes • Urge urinary incontinence episodes Safety: Adverse events, vital signs, and laboratory values were assessed as safety parameters.
Statistical Methods:	Efficacy (Primary): The primary efficacy variables were planned to be summarized by mean, standard deviation, minimum, median, maximum and number of observations. These variables were planned to be reported per visit and together with their corresponding change values. Efficacy (Secondary): Quantitative variables were planned to be summarized by mean, standard deviation, minimum, median, maximum and number of observations. Categorical variables were planned to be summarized by absolute and relative frequencies. Secondary efficacy variables were

	also planned to be reported per visit and together with their corresponding change values. Safety: Treatment groups were planned to be compared with respect to the incidence rates of premature termination, adverse events and concomitant medication use. Laboratory variables were also planned to be obtained. Measurements and changes from baseline in vital signs (blood pressure and pulse rate), and continuous laboratory variables were also obtained.
Number of Subjects:	A total of 40 evaluable subjects were planned, 13 were enrolled, and 7 eligible subjects were valid for safety evaluations.

Study Results

Results Summary — Subject Disposition and Baseline

Two male and five female white subjects with mean age of 51.6 years (range: 29 - 68), and mean body mass index (BMI) of 26.2 kg/m^2 (range: 21.0 - 34.9) were enrolled in this study. All subjects received the study medication and were therefore valid for safety evaluation. All seven subjects were included into the analysis of safety. One subject terminated the study prematurely due to non-compliance with the study medication.

Results Summary — Efficacy

Due to the low number of evaluable subjects, no analysis of efficacy data was performed.

Results Summary — Safety

No deaths or other serious adverse events were reported in this study. No subject discontinued the study treatment due to an adverse event.

Two subjects (28.6%) in the study reported a total of nine adverse events, whereas eight treatment-emergent adverse events (dry mouth, urinary tract infection, headache, micturition urgency and epistaxis [reported 4 times]) were reported by one subject and one non-treatment-emergent adverse event (rhinitis allergic) by another subject. The onset of all adverse events occurred during treatment with darifenacin 7.5 mg.

Two adverse events, dry mouth and headache, were judged to be drug-related by the investigator.

The intensity of all adverse events was reported as mild except for urinary tract infection, which was of moderate intensity.

No clinically significant abnormal laboratory values were detected during the study.

Darifenacin at both dosages was well tolerated.

Conclusion(s)

In this study, the efficacy analysis by means of biometrical tests could not be performed because of lacking data, as the study was prematurely terminated because of insufficient feasibility of the study design. Darifenacin was well tolerated at both the dosages (7.5 mg and 15 mg).

Publication(s):	None		
Date Created or Date Last Updated:	08 MAY 2012	Date of Clinical Study Report:	26 SEP 2008

Investigational Site List

Marketing Authorization Holder in Germany	
Name	Novartis Europharm Ltd.
Postal Address	
Sponsor in Germany	
Legal Entity Name	Bayer HealthCare AG
Postal Address	D-51368 Leverkusen, Germany

List of Investigational Sites

No	Facility Name	Street	ZIP Code	City	Country
1	Kliniken Maria Hilf GmbH	Krankenhaus St. Franziskus Klinik für Urologie Viersener Straße 450	41063	Mönchengladbach	GERMANY
2	Marienhospital Herne Klinik Börnig	Urologische Klinik Widumer Straße 8	44627	Herne	GERMANY
3	Praxis Dr. Stefan Carl & Dr. Achim Forth	Karl-Friedrich-Str. 55	79312	Emmendingen	GERMANY
4	Praxis Drs. Tim Schneider /B. Schneider	Praxisklinik Urologie Rhein/Ruhr Schulstr. 11	45468	Mülheim	GERMANY
5	Universitätsklinikum Hamburg Eppendorf (UKE)	Klinik und Poliklinik für Neurologie Haus S 10 Martinistraße 52	20246	Hamburg	GERMANY
6	Urologische Klinik München-Planegg	Germeringer Str. 32	82152	Planegg	GERMANY