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:	12670	NCT00828971 EudraCT number: 2007-001491-36
Study Phase:	IIIb	
Official Study Title:	A prospective, randomized, open label, active comparator, multicenter, national trial to compare the efficacy and safety of sequential IV/PO moxifloxacin 400 mg once daily versus IV amoxicillin/clavulanate 2,0/0,2 g every 8 hours followed by oral amoxicillin/clavulanate 875/125 mg every 8 hours in the treatment of adult subjects with complicated skin and skin structure infections.	
Therapeutic Area:	Anti-Infectives	
Test Product		
Name of Test Product:	Moxifloxacin (Avelox, BAY12-8039)	
Name of Active Ingredient:	Moxifloxacin HCL	
Dose and Mode of Administration:	Moxifloxacin 400 mg (1.6 mg/mL) in 250 ml solution for infusion intravenously (IV) every 24 hours followed by moxifloxacin 400 mg per oral (PO) 0.16% tablets every 24 hours.	
Reference Therapy/Placebo		
Reference Therapy:	Amoxicillin/clavulanate acid	
Dose and Mode of Administration:	Amoxicillin/clavulanate 2000/200 mg powder for reconstitution in 100 ml of sterile water for injections or other solutions for infusion (i.e. sodium chloride solution 0.9%) administered IV every 8 hours followed by amoxicillin/clavulanate 875/125 mg oral tablets every 8 hours.	
Duration of Treatment:	From a minimum of 7 days to a maximum of 21 days at the discretion of the investigator.	
Studied period:	**Date of first subjects' first visit:**	12 NOV 2008
	Date of last subjects' last visit:	15 OCT 2009
Premature Study Suspension/Termination	The study was terminated on 15 OCT 2009 due to low enrollment.	
Substantial Study Protocol Amendments:	The study was conducted according to study protocol latest version from 13 MAR 2007, and included no substantial amendments.	
Study Center(s):	5 investigational sites enrolled patients in Italy.	

Methodology:	A prospective, randomized, open label, active comparator and multicenter national trial. Treatment duration was aimed of a minimum of 7 days and a maximum of 21 days and followed up until day 14 to day 21 after end of therapy with the study medication. Assessment period consists of: pre-treatment period, treatment period and post-treatment period. Clinical assessments was performed at visit Day 3-5, at end of therapy (EOT) visit (Day 7-21) and finally at test of cure (TOC) visit (14 to 21 days after the End of Treatment). On day 3-5 the clinical response was graded as improvement, failure, indeterminate. At EOT visit the clinical response was graded as resolution, failure, indeterminate. At TOC visit the clinical response was graded as cure, failure, indeterminate. Clinical status, therapeutic effect of the study drug(s), evidence of adverse events and vital signs were recorded daily. Concomitant medications and any therapeutic adjunct/diagnostic or therapeutic interventions were recorded in the case report form (CRF). Bacteriologial response were automatically derived from the result of cultures taken before during and after therapy. At EOT visit the bacteriological response was graded as eradication, presumed eradication, persistence, presumed persistence, indeterminate, super infection and colonisation. Laboratory tests (haematology, biochemistry) have been carried out at Day 3-5. Vital signs, general physical examination and examination of the infection lesion, microbiological examination and laboratory examinations have been undertaken during EOT. If wound material could be obtained at the EOT visit, it was cultured and tested in line. The Test-of-Cure evaluation occurred 14 to 21 days after the end of treatment with study medication. Type of patients: subjects with complicated skin and skin structure infections.
Indication/ Main Inclusion Criteria:	1) Men or women of age >= 18 years with a diagnosis of bacterial skin and skin structure infection that requires: hospitalization; initial parenteral therapy; Complicated by at least one of of following criteria: • Involvement of deep soft tissues (e.g. fascial, muscle layers) • Requirement for a significant surgical intervention including surgical drainage, drainage procedure guided by imaging and/or debridment • Association with a significant underlying disease that may complicate response to treatment. • Presence of SIRS (Systemic Inflammatory Response Syndrome). 2) Duration of infection < 21 days 3) Diagnosis of one of the skin and skin structure infection 4) Presence of at least 3 of pre-defined local signs and symptoms 5) Specimen obtained for culture from infected needle aspiration of purulent material or by tissue biopsy curettage of the surface of the ulcer within 24 hours prior to the initiation of study drug therapy

Study Objectives:	**Overall:** Comparing the efficacy and safety of two sequential (IV/PO) treatment regimens for the treatment of adult subjects with complicated skin and skin structure infections (cSSSIs): - moxifloxacin 400 mg IV, moxifloxacin 400 mg PO - amoxicillin/clavulanate 2000/200 mg IV, amoxicillin/clavulanate 875/125 mg PO
Evaluation Criteria:	**Efficacy (Primary):** Clinical response at the Test-of-Cure Visit 14-21 days afer last dose of study medication. The clinical assessment was made by the investigator at the TOC visit. **Efficacy (Secondary):** Clinical response assessed by the investigator on treatment Day 3-5. Clinical reposnse assessed by the investigator at the End-of-Therapy. Time to switch from oral to IV therapy. Bacteriological response at EOT and at the TOC visit. **Safety:** Type and frequency of adverse events, laboratory data and electrocardiogram (ECG) findings.

Statistical Methods:	Below statistical methods were defined in protocol. **Efficacy (Primary) - if applicable:** Two types of efficacy analyses have to be performed on each efficacy variable, a valid per-protocol and an intention-to-treat analysis. For success rates a 95% confidence interval of the difference of two clinical success rates (treatment group minus comparator group) has been calculated using Mantel-Haenszel weight based on the 10 strata related to cSSSI subtype and presence/absence of Systemic Inflammatory Response Syndrome (SIRS). If lower limit of this confidence interval (CI) is greater than -20%, it is proven that moxifloxacin is clinically not less effective than comparator treatment regimen. If lower limit of this CI is greater than 0, superiority of moxifloxacin is proven. **Efficacy (Secondary) - if applicable:** Clinical response as assessed by the investigator at end of treatment, clinical response at end of treatment and Test-of-Cure in subjects with bacteriologically proven complicated skin and skin structure infection have to be analyzed exploratively in the same way as the primary efficacy variable. **Safety:** Tabulations of the type and frequancy of all adverse events (AEs), vital signs, all laboratory data and ECG data have to be analyzed descriptively.
Number of Subjects:	A total of 368 patients (184 in each treatment arm) were planned to be enrolled to reach a minimum of 276 evaluable patients. The study was terminated on 15 OCT 2009 due to enrollment's problem (lack of enrollment). From first patient enrolled (12 NOV 2008) to study termination a total of 16 patients were recruited and all of them were randomized: 9 patients were treated with amoxicillin/clavulanate and 7 patients with moxifloxacin. Analysis for population, patients' validation and protocol violations have not been done due to the small number of patients data available.
Study Results	
Results Summary — Subject Disposition and Baseline	

A total of 16 patients were enrolled into the study; 12 of them were male and 4 female, and the age average was 48 years (standard deviation [SD] =16.48). All patients were randomized, 9 to amoxicillin/clavulanate (56% male and 44% female, age average equal to 48 (SD=16), 11% asian and 89% white) and 7 to moxifloxacin (100% male, age average equal to 49 (SD=14), 14% asian and 86% white).
3 patients in amoxicillin/clavulanate group dropped out, in 2 cases for lack of efficacy and 1 patient was lost to follow-up. In moxifloxacin group 1 patient dropped out due to lack of efficacy and 1 patient due to concomitant disease (extrapulmonary tuberculosis).
However, in amoxicillin/clavulanate group, all drop out patients obtained a clinical response assessment on Day 3-5: 2 patients were assessed as clinically improved while 1 patient was a clinical failure. On moxifloxacin group only 1 patient receive a clinical response assessment on Day 3-5 (improvement).
On amoxicillin/clavulanate group 6 patients completed all study period whereas on moxifloxacin group only 5 patients completed the study. For all completed patients the clinical response assesment, according to the protocol, was "resolution" for EOT and "cure" for TOC.
The day average at EOT and TOC for amoxicillin/clavulanate is respectively 20 days (SD=6) and 35 days (SD=9), while for moxifloxacin is 25 days (SD=5) and 44 days (SD=6).

Results Summary — Efficacy

As the study was terminated due to lack of recruiment, efficacy evaluation was not performed.

Results Summary — Safety

In amoxicilline/clavulanate group 2 patients suffered from a non serious adverse event each (mild diarrhoea judged as study's treatment related and one headache episode of mild intensity judged as not releted to treatment and resolved).

In amoxicilline/clavulanate group two suffered from one serious adverse event (SAE) each. In one case patient died due to acute pulmonary oedema judged as not related to study treatment and one patient suffered from a severe muscle hemorragia also judged as not releted and resolved at the end of study.

No AE or SAE were reported in Moxifloxacin group.

Laboratory data and ECG findings were not analyzed due to small number of patients.

Conclusion(s)

As the study was terminated due to lack of recruitment any conclusion can not be done.

Publication(s):	None
Date Created or Date Last Updated:	25 June 2013

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Avelox [i.v]
Brand/Trade Name(s) ex-US	Actira®, Avalox®, Avelox®, Izilox®, Megaxin®, Octegra® , Proflox®
Generic Name	Moxifloxacin
Main Product Company Code	BAY12-8039
Other Company Code(s)	n/a
Chemical Description	1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.
Other Product Aliases	n/a

Date of last Update/Change: 11 September 2013

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Avelox [*Oral formulation*]
Brand/Trade Name(s) ex-US	Avelon® Avelox® Avalox® Actira® Octegra® Izilox® Megaxin® Proflox® Promira®
Generic Name	Moxifloxacin
Main Product Company Code	BAY12-8039
Other Company Code(s)	n/a
Chemical Description	1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.
Other Product Aliases	n/a

Date of last Update/Change: 19 Mar 2014