ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 10/09/2014

ClinicalTrials.gov ID: NCT00520403

Study Identification

Unique Protocol ID:	ML19983
Brief Title:	A Study of Avastin (Bevacizumab) in Combination With Standard Therapy in Patients With Metastatic Renal Cell Cancer.
Official Title:	An Open-label Study to Assess the Effect of First-line Treatment With Avastin in Combination With Standard Therapy on Progression-free Survival in Patients With Metastatic Renal Cell Cancer.
Secondary IDs:	

Study Status

Record Verification:	October 2014
Overall Status:	Completed
Study Start:	September 2007
Primary Completion:	March 2010 [Actual]
Study Completion:	March 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: EK 5 528/06 Board Name: Ethik-Kommission des Landes Berlin Board Affiliation: Unknown Phone: +49 30 9012 - 7637 Email: sabine.poeprzyk@lageso.verwaltung-berlin.de
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Germany: Landesamt fur Gesundheit und Soziales Berlin

Study Description

Brief Summary:	This single arm study will assess the efficacy and safety of Avastin in combination with interferon alfa-2a and vinblastine as first line treatment in patients with metastatic renal cell cancer. Patients will receive Avastin (15mg/kg iv) every 3 weeks, interferon alfa-2a 3 times weekly (3 Mio IU sc escalating to 18 Mio sc) and vinblastine (0.1mg/kg iv) every 3 weeks. The anticipated time on study treatment is until tumor progression, and the target sample size is 100-500 individuals.
Detailed Description:	

Conditions

Conditions:	Renal Cell Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	25 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: bevacizumab [Avastin] 15mg/kg iv every 3 weeks Drug: Interferon alfa-2a 3 MioIU sc escalating to 18 MioIU sc, 3 times weekly Drug: Vinblastine 0.1mg/kg iv every 3 weeks

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age;
- metastatic renal cell cancer of predominantly clear cell type;
- >=1 measurable lesion.

Exclusion Criteria:

- prior treatment with chemotherapy, cytokine or tyrosine kinase inhibitor therapy for metastatic renal cell cancer;
- ongoing or recent need for full therapeutic dose of anticoagulants or chronic daily treatment with aspirin (>325mg/day);
- clinically significant cardiovascular disease.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Germany
Berlin, Germany, 10117

Leipzig, Germany, 04103

Weiden, Germany, 92637

Jena, Germany, 07743

Halle, Germany, 06097

Kassel, Germany, 34125

Rehling, Germany, 86058

Dessau, Germany, 06846

Berlin, Germany, 10967

Magdeburg, Germany, 39120

Frankfurt, Germany, 60596

Stuttgart, Germany, 70174

Hannover, Germany, 30449

Erlangen, Germany, 91052

Bremen, Germany, 28277

Kiel, Germany, 24105

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Bevacizumab + Interferon Alfa-2a (IFN)/Vinblastine	Cycle 1 (3-week cycle): Participants received vinblastine sulfate 0.1 mg/kg intravenously (IV) and bevacizumab 15 milligrams per kilogram (mg/kg) IV on Day 1 followed by 2 weeks off and IFN subcutaneous (SC) injection three times per week (starting on Day 1) at doses of 3 million International Units (mIU) (Week 1), 9 mIU (Week 2), and 18 mIU (Week 3). Cycles 2 to 17 (3-week cycles): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN 18 mIU SC injection three times per week during Weeks 1 through 3; the cycle was repeated every 3 weeks up to Week 51 (Cycle 17) or to tumor progression. If the first 17 cycles were tolerated without tumor progression, participants received bevacizumab monotherapy: bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off; this cycle was repeated every 3 weeks up to Week 102 (Cycle 34) or to tumor progression.

Bevacizumab + IFN/Vinblastine

	Bevacizumab + Interferon Alfa-2a (IFN)/Vinblastine
Started	25
Completed	7
Not Completed	18
Radiological progression of cancer	6
Adverse Event	4
Withdrawal of consent	4
Death	2
Discontinuation of study/background drug	1
Protocol Deviation affecting safety	1

Bevacizumab Monotherapy

	Bevacizumab + Interferon Alfa-2a (IFN)/Vinblastine
Started	2 [1]
Completed	0

	Bevacizumab + Interferon Alfa-2a (IFN)/Vinblastine
Not Completed	2
Radiological progression of cancer	1
Symptomatic progression of cancer	1

[1] 2 of 7 participants completing Bevacizumab+IFN/vinblastine cycles initiated bevacizumab monotherapy

Baseline Characteristics

Analysis Population Description

Safety Population: included all participants, even those who withdrew from the study prematurely and who received at least 1 dose of bevacizumab and had a safety follow-up visit.

Reporting Groups

	Description
Bevacizumab + IFN/Vinblastine	Cycle 1 (3-week cycle): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN SC injection three times per week (starting on Day 1) at doses of 3 mIU (Week 1), 9 mIU (Week 2), and 18 mIU (Week 3). Cycles 2 to 17 (3-week cycles): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN 18 mIU SC injection three times per week during Weeks 1 through 3 (starting on Day 1); the cycle was repeated every 3 weeks up to Week 51 (Cycle 17) or to tumor progression. If the first 17 cycles were tolerated without tumor progression, participants received bevacizumab monotherapy: bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off; this cycle was repeated every 3 weeks up to Week 102 (Cycle 34) or to tumor progression.

Baseline Measures

	Bevacizumab + IFN/Vinblastine
Number of Participants	25
Age, Continuous [units: years] Mean (Standard Deviation)	62.2 (8.5)
Gender, Male/Female [units: participants]	
Female	4
Male	21

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression or Death
Measure Description	Disease progression was evaluated according to the Response Evaluation Criteria In Solid Tumors (RECIST) using computed tomography (CT) scans (preferred method), magnetic resonance imaging (MRI) scans, X-ray, bone scans, or clinical examination.
Time Frame	Days 0, 91, 182, 273, 365, 456, and 547
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: all participants, even those who withdrew from the study prematurely, who received at least 1 dose of study medication and for whom the primary efficacy variable was measured at least once during the time when the participant received study medication.

Reporting Groups

	Description
Bevacizumab + IFN/Vinblastine	Cycle 1 (3-week cycle): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN SC injection three times per week (starting on Day 1) at doses of 3 mIU (Week 1), 9 mIU (Week 2), and 18 mIU (Week 3). Cycles 2 to 17 (3-week cycles): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN 18 mIU SC injection three times per week during Weeks 1 through 3 (starting on Day 1); the cycle was repeated every 3 weeks up to Week 51 (Cycle 17) or to tumor progression. If the first 17 cycles were tolerated without tumor progression, participants received bevacizumab monotherapy: bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off; this cycle was repeated every 3 weeks up to Week 102 (Cycle 34) or to tumor progression.

Measured Values

	Bevacizumab + IFN/Vinblastine
Number of Participants Analyzed	17
Percentage of Participants With Disease Progression or Death [units: percentage of participants]	66.9

2. Primary Outcome Measure:

Measure Title	PFS - Time to Event
Measure Description	PFS was defined as the time in days from the date of treatment start to the date of first documented disease progression or death. Disease progression was evaluated according to RECIST using CT scans (preferred method), MRI scans, X-ray, bone scans, or clinical examination. Median PFS was estimated using the Kaplan-Meier method
Time Frame	Days 0, 91, 182, 273, 365, 456, and 547
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Bevacizumab + IFN/Vinblastine	Cycle 1 (3-week cycle): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN SC injection three times per week (starting on Day 1) at doses of 3 mIU (Week 1), 9 mIU (Week 2), and 18 mIU (Week 3). Cycles 2 to 17 (3-week cycles): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN 18 mIU SC injection three times per week during Weeks 1 through 3 (starting on Day 1); the cycle was repeated every 3 weeks up to Week 51 (Cycle 17) or to tumor progression. If the first 17 cycles were tolerated without tumor progression, participants received bevacizumab monotherapy: bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off; this cycle was repeated every 3 weeks up to Week 102 (Cycle 34) or to tumor progression.

Measured Values

	Bevacizumab + IFN/Vinblastine
Number of Participants Analyzed	17
PFS - Time to Event [units: days] Median (Standard Error)	274 (31.6)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Objective Response (OR)
Measure Description	Percentage of participants with OR based on assessment of confirmed complete remission (CR) or confirmed partial remission (PR) according to RECIST.

Time Frame	Baseline and Cycles 3, 6, 9, 13, and 17
Safety Issue?	No

Analysis Population Description

ITT Population; missing data were imputed using the last observation carried forward (LOCF) technique. Number (n) equals (=) number of participants assessed at each specific visit.

Reporting Groups

	Description
Bevacizumab + IFN/Vinblastine	Cycle 1 (3-week cycle): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN SC injection three times per week (starting on Day 1) at doses of 3 mIU (Week 1), 9 mIU (Week 2), and 18 mIU (Week 3). Cycles 2 to 17 (3-week cycles): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN 18 mIU SC injection three times per week during Weeks 1 through 3 (starting on Day 1); the cycle was repeated every 3 weeks up to Week 51 (Cycle 17) or to tumor progression. If the first 17 cycles were tolerated without tumor progression, participants received bevacizumab monotherapy: bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off; this cycle was repeated every 3 weeks up to Week 102 (Cycle 34) or to tumor progression.

Measured Values

	Bevacizumab + IFN/Vinblastine
Number of Participants Analyzed	17
Percentage of Participants With Objective Response (OR) [units: percentage of participants]	
Week 9 (n=14)	21.4
Week 18 (n=16)	31.3
Week 27 (n=16)	37.5
Week 39 (n=16)	31.3
Week 51 (n=16)	31.3

4. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)

Measure Description	OS was defined as the duration from treatment start to death from any cause. Overall survival was censored at the last contact for surviving participants and missing data points.
Time Frame	Baseline, Day 1 of every cycle to disease progression or death (up to Week 102)
Safety Issue?	No

Analysis Population Description

Two of 25 participants died during the course of the study, thus, median overall survival could not be analyzed.

Reporting Groups

	Description
Bevacizumab + IFN/Vinblastine	Cycle 1 (3-week cycle): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN SC injection three times per week (starting on Day 1) at doses of 3 mIU (Week 1), 9 mIU (Week 2), and 18 mIU (Week 3). Cycles 2 to 17 (3-week cycles): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN 18 mIU SC injection three times per week during Weeks 1 through 3 (starting on Day 1); the cycle was repeated every 3 weeks up to Week 51 (Cycle 17) or to tumor progression. If the first 17 cycles were tolerated without tumor progression, participants received bevacizumab monotherapy: bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off; this cycle was repeated every 3 weeks up to Week 102 (Cycle 34) or to tumor progression.

Measured Values

	Bevacizumab + IFN/Vinblastine
Number of Participants Analyzed	25
Overall Survival (OS) [units: weeks] Median (Full Range)	NA (NA to NA) [1]

[1] Median could not be calculated due to lack of events as only 2 of 25 participants died during the course of the study.

Reported Adverse Events

Time Frame	From treatment start to 28 days after treatment cessation in the regular treatment period only (Cycles 1 through 17; bevacizumab + IFN/vinblastine). Does not include AEs reported during bevacizumab monotherapy (Cycles 18 and beyond).

Additional Description	AE (serious and non-serious) information was collected for participants in the Safety Population and reported for the regular treatment period only (Cycles 1 through 17; bevacizumab + IFN/vinblastine).

Reporting Groups

	Description
Bevacizumab + IFN/Vinblastine	Cycle 1 (3-week cycle): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN SC injection three times per week (starting on Day 1) at doses of 3 mIU (Week 1), 9 mIU (Week 2), and 18 mIU (Week 3). Cycles 2 to 17 (3-week cycles): Participants received vinblastine sulfate 0.1 mg/kg IV and bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off and IFN 18 mIU SC injection three times per week during Weeks 1 through 3 (starting on Day 1); the cycle was repeated every 3 weeks up to Week 51 (Cycle 17) or to tumor progression. If the first 17 cycles were tolerated without tumor progression, participants received bevacizumab monotherapy: bevacizumab 15 mg/kg IV on Day 1 followed by 2 weeks off; this cycle was repeated every 3 weeks up to Week 102 (Cycle 34) or to tumor progression.

Serious Adverse Events

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Total	8/25 (32%)
Blood and lymphatic system disorders	
Neutropenia [A] *	1/25 (4%)
Gastrointestinal disorders	
Abdominal Pain [A] *	1/25 (4%)
Nausea [A] *	1/25 (4%)
Vomiting [A] *	1/25 (4%)
General disorders	
Chest Pain [A] *	1/25 (4%)
General Physical Health Deterioration [A] *	1/25 (4%)
Injection Site Reaction [A] *	1/25 (4%)
Systemic Inflammatory Response Syndrome [A] *	1/25 (4%)

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Metabolism and nutrition disorders	
Dehydration [A] *	1/25 (4%)
Nervous system disorders	
Cerebral Haemorrhage [A] *	1/25 (4%)
Renal and urinary disorders	
Proteinuria [A] *	1/25 (4%)
Respiratory, thoracic and mediastinal disorders	
Dyspnoea [A] *	1/25 (4%)
Pulmonary Embolism [A] *	1/25 (4%)
Vascular disorders	
Hypertension [A] *	1/25 (4%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (10.1)

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Total	22/25 (88%)
Blood and lymphatic system disorders	
Anaemia [A] *	1/25 (4%)
Leukopenia [A] *	3/25 (12%)
Neutropenia [A] *	1/25 (4%)
Pancytopenia [A] *	1/25 (4%)
Cardiac disorders	

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Arrhythmia [A] *	1/25 (4%)
Tachycardia [A] *	2/25 (8%)
Ear and labyrinth disorders	
Vertigo [A] *	2/25 (8%)
Gastrointestinal disorders	
Abdominal pain lower [A] *	1/25 (4%)
Constipation [A] *	1/25 (4%)
Diarrhoea [A] *	2/25 (8%)
Dyspepsia [A] *	2/25 (8%)
Ileus paralytic [A] *	1/25 (4%)
Loose tooth [A] *	1/25 (4%)
Nausea [A] *	7/25 (28%)
Periodontitis [A] *	1/25 (4%)
Stomatitis [A] *	1/25 (4%)
Tongue ulceration [A] *	1/25 (4%)
Toothache [A] *	1/25 (4%)
Vomiting [A] *	2/25 (8%)
General disorders	
Asthenia [A] *	1/25 (4%)
Chills [A] *	5/25 (20%)
Drug intolerance [A] *	1/25 (4%)
Fatigue [A] *	10/25 (40%)

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Impaired healing [A] *	1/25 (4%)
Influenza like illness [A] *	6/25 (24%)
Mucosal inflammation [A] *	4/25 (16%)
Pyrexia [A] *	3/25 (12%)
Infections and infestations	
Abscess jaw [A] *	1/25 (4%)
Lung infection [A] *	1/25 (4%)
Nasopharyngitis [A] *	1/25 (4%)
Otitis media [A] *	1/25 (4%)
Urinary tract infection [A] *	1/25 (4%)
Injury, poisoning and procedural complications	
Postoperative hernia [A] *	1/25 (4%)
Wound [A] *	1/25 (4%)
Investigations	
Blood sodium decreased [A] *	1/25 (4%)
Intraocular pressure test [A] *	1/25 (4%)
Urine output decreased [A] *	1/25 (4%)
Weight decreased [A] *	3/25 (12%)
Metabolism and nutrition disorders	
Anorexia [A] *	10/25 (40%)
Hyponatraemia [A] *	1/25 (4%)
Iron deficiency [A] *	2/25 (8%)
Musculoskeletal and connective tissue disorders	

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Arthralgia [A] *	4/25 (16%)
Back pain [A] *	4/25 (16%)
Bursitis [A] *	1/25 (4%)
Fascial hernia [A] *	1/25 (4%)
Groin pain [A] *	1/25 (4%)
Musculoskeletal chest pain [A] *	1/25 (4%)
Myalgia [A] *	1/25 (4%)
Osteonecrosis [A] *	1/25 (4%)
Pain in extremity [A] *	4/25 (16%)
Nervous system disorders	
Dizziness [A] *	3/25 (12%)
Dysgeusia [A] *	3/25 (12%)
Headache [A] *	6/25 (24%)
Peripheral sensory neuropathy [A] *	1/25 (4%)
Tremor [A] *	1/25 (4%)
Psychiatric disorders	
Depressed mood [A] *	2/25 (8%)
Depression [A] *	1/25 (4%)
Insomnia [A] *	2/25 (8%)
Restlessness [A] *	1/25 (4%)
Sleep disorder [A] *	1/25 (4%)
Renal and urinary disorders	

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Proteinuria [A] *	8/25 (32%)
Renal failure [A] *	1/25 (4%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] *	1/25 (4%)
Dysphonia [A] *	2/25 (8%)
Dyspnoea [A] *	4/25 (16%)
Epistaxis [A] *	6/25 (24%)
Nasal dryness [A] *	1/25 (4%)
Nocturnal dyspnoea [A] *	1/25 (4%)
Pleural effusion [A] *	1/25 (4%)
Pneumothorax [A] *	1/25 (4%)
Rhinorrhoea [A] *	1/25 (4%)
Skin and subcutaneous tissue disorders	
Alopecia [A] *	1/25 (4%)
Dry skin [A] *	2/25 (8%)
Nail disorder [A] *	1/25 (4%)
Pruritus [A] *	1/25 (4%)
Scar pain [A] *	2/25 (8%)
Skin atrophy [A] *	1/25 (4%)
Urticaria [A] *	1/25 (4%)
Vascular disorders	
Haemorrhage [A] *	1/25 (4%)

	Bevacizumab + IFN/Vinblastine
	Affected/At Risk (%)
Hypertension [A] *	6/25 (24%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (10.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

Results Point of Contact:

Name/Official Title: Medical Communications
Organization: Hoffmann-LaRoche
Phone: 800-821-8590
Email: genentech@druginfo.com