POLARIS STUDY PROTOCOL SYNOPSIS

Study title	A non-interventional study in patients with diabetic macula edema (DME) with central involvement to assess the effectiveness of existing anti vascular endothelial growth factor (anti-VEGF) treatment regimens
Protocol Version / Date of synopsis	V2.0 / 12 Feb 2013
Study sponsor	Bayer Healthcare AG
Study phase	Not applicable
Study number	Impact Number 16459 NIS Project Code NN1201
Therapeutic area	Ophthalmology
Name of product	Not applicable
Name of active ingredient	Not applicable
Dose and mode of administration	Not applicable
Reference therapy	Approved intravitreal anti-VEGF therapy
Dose and mode of administration	Decision made at the discretion of the attending investigator
Duration of treatment	Decision made at the discretion of the attending investigator
Study design / methodology	This non-interventional, multi-center study collects data on patients with DME who are treated with an approved intraviteal anti-VEGF therapy (ranibizumab). The observation period starts October 01, 2012. Patients who received the first treatment with an approved intravitreal anti-VEGF therapy from October 01, 2012 must be consecutively screened and, if eligible, enrolled. Patients will be followed up for a time-period of 12 months or until it is no longer possible. For each patient, the investigator or a delegate collects data as defined in the case report form at an initial visit, follow-up visits and final visit, where available. Sponsor or contract research organization may audit data by source data verification.
Indication/ **Main inclusion criteria**	INCLUSION CRITERIA: Patients diagnosed with type 1 or 2 diabetes mellitus and DME with central involvement (defined as the area of the center subfield of optical coherence tomography [OCT]) treated with an approved intravitreal anti-

	VEGF therapy in routine practice. The diagnosis and treatment decision is made at the discretion of the attending investigator, prior to enrollment into the study. The initial visit must be at or after October 01, 2012. Where applicable, patients must give informed consent in writing. EXCLUSION CRITERIA: Patients are not to be enrolled if they were treated with any anti-VEGF therapy in the past before start of the observation period (October 01, 2012) or enrolment into the study, respectively and / or if they are participating in an investigational program with interventions out of clinical routine practice.
Study objectives	PRIMARY OBJECTIVE(S): To evaluate changes in visual acuity (ETDRS/Snellen) based on clinical management patterns and resource utilization in patients with DME with central involvement starting treatment with an approved intravitreal anti-VEGF therapy. SECONDARY OBJECTIVE(S): ▪ To determine influencing factors for visual acuity changes. ▪ To determine how disease activity is monitored in real-life clinical settings for DME. ▪ To measure the severity of DME with central involvement. ▪ To determine the socio-demographic profile of the patients suffering from DME. ▪ To determine Quality of Life (QoL; only prospectively enrolled patients and where applicable).
Evaluation criteria	PRIMARY: Changes in visual acuity in patients with DME starting treatment with an approved intravitreal anti-VEGF therapy will be evaluated including assessments of the following procedures: ▪ Eye clinic visits (both monitoring and treatment visits) ▪ Number of intravitreal anti-VEGF injections ▪ Visual acuity test (ETDRS/ Snellen)
Evaluation criteria	SECONDARY: ▪ Demographic and clinical characteristics of patients included in the study ▪ Mean time from diagnosis to first commencement with an approved intravitreal anti-VEGF therapy ▪ Resource utilization in terms of treatment choices, frequency and duration ▪ Mean change of visual acuity from start of intravitreal anti-

	VEGF therapy to each analysis time point and end of follow-up time points ▪ Mean change of retinal thickness from start of intravitreal anti-VEGF therapy to each analysis time point and end of follow-up time points ▪ Presence of clinically significant macular edema (CSME) from start of intravitreal anti-VEGF therapy to each analysis time point and end of follow-up time points ▪ Proportion of patients requiring pan-retinal/focal/grid laser or other adjuvant/additional disease related therapy ▪ Subgroup analysis according to pathological and follow-up patterns ▪ Mean change in quality of life score, using the NEI VFQ-25 (only prospectively enrolled patients and where applicable)
Plan for statistical analysis	All variables will be analyzed descriptively with appropriate statistical methods: continuous variables by descriptive statistics (i.e. mean, standard deviation, median, quartiles, minimum and maximum) and categorical variables by frequency tables (absolute and relative frequencies). Number of patients with missing data is presented as separate category. For the primary analysis the mean change from baseline in visual acuity and a 95% confidence interval will be calculated. Moreover, the statistical analysis will include a description of demographic data, clinical findings and visual evolution. To determine follow-up and management patterns of patients with DME with central involvement, tests and interventions for diagnosis and follow-up will be described. For resource utilization, the number of injections and the frequency of monitoring the disease activity in real-life will be evaluated. Whenever reasonable, data will be stratified by subgroups (i.e. age, gender, other baseline characteristics). For coding of verbatim documentation, the following coding systems are applied: Concomitant therapies with WHO DD, concomitant diseases and Adverse Events with MedDRA.
Number of patients	807 in approximately 80 sites worldwide in 9 countries