Science For A Better Life

Clinical Study Synopsis

This Clinical Study Synopsis is provided for patients and healthcare professionals to increase the transparency of Bayer's clinical research. This document is not intended to replace the advice of a healthcare professional and should not be considered as a recommendation. Patients should always seek medical advice before making any decisions on their treatment. Healthcare Professionals should always refer to the specific labelling information approved for the patient's country or region. Data in this document or on the related website should not be considered as prescribing advice.
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.

Title	Incidence of Second primary MAlignancies in pRostate Cancer patients with bOne metastases – an observational retrospective cohort study in Sweden (SMARCOS)
Keywords	Bone metastases; Castration resistant; Observational study; Prostate cancer; Second primary malignancy
Rationale and background	The development of bone metastases in prostate cancer is a serious threat to the patients' quality of life and survival. Radium-223 is a new treatment for metastatic castration-resistant prostate cancer that selectively targets bone metastases with high-energy, short-range alpha particles. Following a feasibility assessment on appropriate external secondary data sources, an epidemiology program was established to evaluate the safety profile of radium-223 in Germany, Sweden and the United States. This SMARCOS study is the Swedish part of the epidemiology program, conducted using the Swedish register databases.
Research question and objectives	The primary objective in this study was to evaluate the incidence of developing any second primary malignancy (including myelodysplastic syndrome/acute myeloid leukaemia and osteosarcoma) among prostate cancer patients with bone metastases (mPC) and among a subgroup for whom the prostate cancer can be considered to be castration-resistant (mCRPC). The secondary objectives in this study were to evaluate the incidences of site-specific second primary malignancies, the overall survival, and to investigate factors affecting the incidence of second primary malignancies.
Study Design	This was an observational retrospective cohort study that employed existing nationwide register data in Sweden.
Setting	Patients were included in the mPC population if they fulfilled the following two criteria: • PC diagnosis in 1 January 1998 – 31 December 2011 • Bone metastases diagnosis in 1 January 1999 – 31 December 2011. Patients were included in the mCRPC population if they fulfilled the following three criteria: • PC diagnosis in 1 January 1998 – 31 December 2011, first bone metastases diagnosis in 1 January 2007 – 31 December 2011. • One of the following in 1 January 2006 – 31 December 2011 and within one month after or any time before bone metastases diagnosis using all available history since the first PC diagnosis: o Discontinuation of the initial chemical castration (Androgen Deprivation Therapy; ADT), change of the agent or modality of ADT, or start of treatment for advanced PC after the primary ADT (including chemotherapy or

	mitoxantrone). o Surgical castration and initiation of ADT treatment (after a grace period of at least 1 month, i.e. 30 days), chemotherapy or mitoxantrone afterwards. o Treatment with medication specific to either CRPC or mCRPC. Patients were excluded from the mPC and mCRPC populations if they fulfilled any of the following criteria: • First PC diagnosis later than 2 months after the diagnosis of bone metastases, or • Permanent residence not in Sweden or patient not otherwise contributing to the registers at least a year before the diagnosis of bone metastases (patient counted not contributing also if database existence less than a year before cohort entry), or • Use of any radiopharmaceuticals for bone metastases at any time.
Subjects and Study Size, including dropouts	Based on a feasibility assessment, it was estimated that 15,000 mPC and 4,060 mCRPC patients would be available for the study. Finally, following the pre-defined inclusion and exclusion criteria, 15,953 and 2,853 patients were included in the actual mPC and mCRPC study populations, respectively.
Variables and Data sources	This study was conducted using the Prostate Cancer data Base Sweden that has data from the National Prostate Cancer Register of Sweden linked with other national healthcare registers. The primary outcome was any second primary malignancy. Secondary outcomes included overall mortality and site-specific second primary malignancies. The main variable adjusted for in the analyses was age.
Results	During the total 32,450 and 2,630 person years in the mPC and mCRPC cohorts, 2,791 and 333 second primary malignancy (SPM) events were observed, respectively. The incidence rates of SPM per 1,000 person years in these cohorts were 86 (95% CI 83, 89) and 127 (95% CI 114, 141), respectively. The median survival in the mPC cohort was crudely 1.5 years (13,965 deaths) and in the mCRPC cohort 0.6 years (2,633 deaths). The respective mean follow-up times were 2.3 and 1.0 years.
Discussion	The estimated incidence rates of second primary malignancies in this study for mPC and mCRPC patients were higher than what can be observed from the overall cancer statistics of Swedish male subjects of the same age. This might indicate that mPC and mCRPC patients in this study were more prone to having second cancers than the general Swedish male population having any cancer. Survival time in the study populations was skewed: some patients

	died soon after CED whereas some survived relatively long despite the metastatic condition.
Marketing Authorisation Holder(s)	[redacted]
Names and affiliations of principal investigators	[redacted]