1. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**
Title of study:	CORDIALLY® - CEE: Characteristics of patients with Type 2 Diabetes treated with modern antidiabetic drugs. A real -world data collection of patient baseline characteristics, treatment patterns and comorbidities in Central Eastern European (CEE) countries		
Keywords:	Type 2 diabetes, SGLT2i, DPP4i, GLP-1 RA, treatment pattern		
Rationale and background:	Cardiovascular Disease (CVD) is the most common cause of mortality in patients with Type 2 Diabetes (T2D). Also, chronic kidney disease (CKD) is associated with increased all-cause mortality, which is substantially higher in patients with a diagnosis of diabetes. Registry outcomes imply that patient characteristics might differ between patients initiating empagliflozin or other glucose lowering drugs. The CORDIALLY® - CEE NIS was conducted to get insights into T2D patient characteristics when initiating different types of T2D treatments under routine conditions, including associated comorbidities (CVD, CKD), concomitant medications and the association of socioeconomic factors with treatment decisions.		

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**
Research question and objectives:	The primary objective was to describe and compare T2D patients' baseline characteristics when initiating either empagliflozin - or other SGLT2i, DPP4i or GLP-1 RA on top of current antidiabetic treatment by different HCP specialties in CEE countries. Secondary objectives were 1. To describe the prevalence of comorbidities [prevalence of cardiovascular disease (CVD), chronic kidney disease (CKD)] in this T2D patient population at index date 1 2. To describe and compare the actual treatment uses at index date 1 in patients with and without established CVD (Established CVD defined as acute myocardial infarction (AMI), cardiology intervention, ischemic heart disease (IHD), congestive heart failure (CHF), peripheral arterial disease (PAD), or stroke) 3. To describe the association of socioeconomic parameters with treatment decisions at index date 1 4. To assess the discontinuation rate, reasons for discontinuation and average duration of treatment for GLP-1 RA, DPP4i and SGLT2i after a follow up of approximately one year from the initial timepoint (= index date 2)		
Study design:	Non-interventional, multi-country, multi-site study based on existing data from medical records of patients initiating treatment with empagliflozin or other SGLT2i, DPP4i or GLP-1 RA in the time period from September 2018 to December 2018 according to the approved label.		

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**
Setting:	Between August 2019 and January 2021, 177 medical offices (endocrinologist, diabetologist or cardiologist) in five CEE countries (Bulgaria, Czech Republic, Hungary, Poland, Russian Federation) participated in the non-interventional study CORDIALLY. Site selection was performed to reflect routine T2D care in the participating countries in order to secure representativeness of the T2D population. The first patient was included on 26 AUG 2019 and the last patient on 14 JAN 2021. First patient first visit (FPFV = index date 1) was on 01 SEP 2018 and last patient last visit (LPLV = index date 2) was on 16 MAR 2021.		
Subjects and study size, including dropouts:	Patients could be included if all of the following criteria were met: 1. Written informed consent prior to participation 2. Female and male patients age ≥18 years 3. Patients with T2D diagnosis 4. Patients who have been newly initiated (first ever use) with empagliflozin or other SGLT2i, DPP4i or GLP-1 RA between September 2018 and December 2018 (study index date 1) 5. Patients have been naïve to treatment with empagliflozin or other SGLT2i, DPP4i or GLP-1 RA at study index date 1		

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**
	Patients fulfilling the following exclusion criteria were excluded from study participation: 1. Patients age <18 years 2. Patients with diagnosis of other types of diabetes than T2D 3. Patients who do not provide written consent to the terms of the study It was planned to include data of approximately 4000 patients. Overall, 4083 patients have been screened. Of these, 4055 patients fulfilled all inclusion and exclusion criteria and had received a first prescription of a respective study medication and thus were included in Prescribed Patient Set (PPS). 3,618 patients of the PPS with a documentation at the study index date 2 could be included in the Full Analysis Set (FAS). Patients of FAS included before the protocol amendment needed an additional signed informed consent for the documentation at index date 2.		
Variables and data sources:	Existing patient data (medical chart review) previously collected by health care professionals during routine documentation in patients treated for T2D were the basis of data collection. The following parameters were collected and assessed at study index date 1:		

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

1. Patient demographics (age, gender, height, weight, BMI, ethnicity)
2. Time since diagnosis of Type 2 Diabetes
3. Clinical parameters relevant for T2D, CVD, CKD assessment (see below) as valid on study index date 1
4. Comorbidities like cardiovascular disease and related risk factors and comorbidities like chronic kidney disease and related risk factors at study index date 1
5. T2D medication the treating physician newly prescribed at study index date 1
6. Concomitant T2D medications at study index date 1
7. Concomitant CVD and CKD medications at index date 1
8. Involvement of other HCPs in treatment decisions at study index date 1
9. Relevant socioeconomic parameters (see below) at index date 1

The following parameters were collected and assessed at study index date 2 (= one year ± 2 months after index date 1):

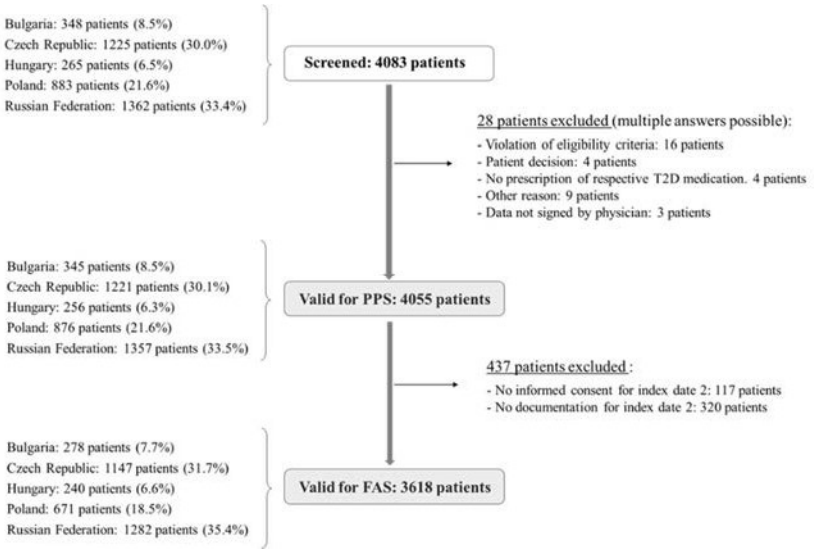
1. Status of T2D medication (continuation / discontinuation)
2. If discontinuation:
   a. stop date of initial (index date 1) T2D medication (if available)
   b. Reason for therapy discontinuation
   c. Involvement of other HCPs in decision for therapy discontinuation

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

Results:

4083 patients were registered by a total of 177 participating medical offices in Bulgaria (15 sites), Czech Republic (58 sites), Hungary (10 sites), Poland (28 sites) and the Russian Federation (66 sites).

Thereof, 4055 patients weres valid for PPS. 3618 patients of PPS had documentation of data at study index date 2 and therefore made up the FAS analysis set:



Regarding total PPS, there were slightly more male than female patients enrolled, 50.9% vs. 49.1%. The great majority were non-black people, only 0.7% were black. Patients were in mean (SD) 63.1 (10.2) years old. A mean (SD) BMI of 32.9 (5.8) kg/m^2 is a hint that enrolled patients had to deal with obesity. Hypertension was present in 84.6% of patients; 52.4%

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

had never smoked and 42.8% were physically active. Greatest share of patients had no family history of early heart or kidney disease. Calculating the 10 years risk for developing fatal CVD resulted in a mean (SD) risk score of 6.4 (5.5) (= high risk). Mean duration (SD) of T2D from date of diagnosis until date of registration amounted to 9.9 (6.9) years for PPS patients. At study index date 1, 30.7% of PPS patients had poorly controlled diabetes with an HbA1c value ≥8.5%.

Initially prescribed T2D medication was mainly empagliflozin (49.5% of PPS and 46.9% of FAS), followed by DPP4i (28.2% of PPS and 29.1% of FAS), other SGLT2i (14.4% of PPS and 14.8% of FAS), and GLP-1 RA (8.9% of PPS and 9.2% of FAS).

Primary Outcome(s): Baseline characteristics at T2D treatment initiation according to HCP specialties in CEE countries- (PPS)

Participating HCPs were endocrinologists, diabetologists and cardiologists, who enrolled 1652, 2301 and 102 patients, respectively. 76.5% of patients registered by cardiologists received prescription of empagliflozin , whereas this drug was prescribed by endocrinologists and diabetologists for 49.3% and 46.6%, respectively, of their included patients. Regarding concomitant medication, about 80% of patients of each HCP specialty received metformin as further T2D medication. Diabetologists had the highest percentage of patients receiving concomitant insulin, namely 28.6%. Share of patients included by cardiologists were higher for each CVD and/or CKD drug than share of patients enrolled by the other two specialties. No statistically significant difference in demographic characteristics between modern T2D medication was observed in patients enrolled by cardiologists. In contrast, age, gender, and BMI was statistically significantly different between T2D medication in patients enrolled by endocrinologists and diabetologists. Both HCP specialties prescribed GLP-1 RA for patients with lowest mean age and highest mean BMI. Regarding time period from T2D diagnosis until first prescription of modern T2D

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

drug by HCP specialties, mean time was about 9 and 10 years for patients in all medication groups enrolled by endocrinologists and diabetologists, respectively. Patients enrolled by cardiologists showed the greatest differences with mean values of 6.0 years for patients in GLP-1 RA medication group and 10.9 years for patients receiving 'Other SGLT2i'. Mean (SD) HbA1c values in patients of endocrinologists, diabetologists and cardiologists amounted to 8.4% (1.3), 8.2% (1.4), and 8.2% (1.4), respectively. Cardiologists had the lowest share of patients in category 'HbA1c ≥8.5%' (19.6%), however 30.4% of their patientshad missing HbA1c values. Most of patients with an HbA1c ≥8.5% received a prescription of empagliflozin irrespective of HCP specialty. Risk factors with known influence on T2D were also analyzed: Overweight, hypertension, tobacco smoking, physical inactivity, and family history for early heart or kidney disease. Endocrinologists and diabetologists had a similar patient distribution regarding risk factors 'BMI' and 'hypertension' within the four T2D medication groups. Among behavioral risk factors, tobacco smoking was the least present one. More patients in all T2D medication groups at each HCP specialty had never smoked than were former or current smokers. In nearly all T2D medication groups at each HCP specialty more than 50% of patients was physically inactive, except for patients of diabetologists receiving empagliflozin and DPP4i with <50% each of physically inactive patients. The greatest share of patients had neither a family history of early heart disease nor of early kidney disease. Endocrinologists treated a greater percentage of patients in each T2D medication group with a family history of early heart disease than diabetologists, about 30% versus about 20%.

Regarding calculated 10 years risk for fatal CVD, patients treated by cardiologists had a higher mean (SD) risk score than patients of endocrinologists or diabetologists, 8.6 (7.5) vs. 6.0 (5.3) or 6.7 (5.5), respectively. Patients of endocrinologists with an empagliflozin

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

prescription had a higher mean risk score than patients with prescription of the other drugs, 6.4 vesus ≤6.0. Patients of diabetologists with prescription of empagliflozin or DPP4i, had a higher mean risk score compared to patients with prescription of GLP-1 RA or other SGLT2i, 7.0 versus ≤6.5. Patients of cardiologists with DPP4i prescription had a higher mean risk score (9.4) than the other T2D medication groups.

Highly relevant reasons for choosing the respective T2D medication was 'HbA1c lowering' (88.7%) for empagliflozin, 'simple dosing / administration' (76.4%) for DPP4i, 'weight loss' (93.3%) for GLP-1 RA, and 'HbA1c lowering' (82.4%) for other SGLT2i by endocrinologists. Diabetologists assessed 'cardiovascular risk reduction' (78.2%) for empagliflozin, and 'HbA1c lowering' each for DPP4i, GLP-1 aRA, and for other SGLT2i with 77.1%, 89.3%, and 83.2%, respectively, as highly relevant for their decision. Cardiologists assessed 'cardiovascular risk reduction' (92.3%) for empagliflozin, 'favourable side effect profile' (81.3%) for DPP4i, all stated reasons for the one patient with prescription of GLP-1 RA, and 'cardiovascular risk reduction' (100.0%) for other SGLT2i as highly relevant for their decision. 'Weight loss' was mainly assessed as 'not relevant at all'. 86.0% of endocrinologists and 90.7% of diabetologists did not involve other physicians in their T2D treatment decision; this was stated by 63.7% of cardiologists.

<u>Secondary Outcome: Burden of comorbidities (prevalence of CVD, CKD and CVD/CKD risk factors) in this T2D patient population at index date 1) – (PPS)</u>

1485 patients (36.6%) of enrolled PPS patients had at least one CVD at study index date. Presence of concomitant CKD was evaluated by 2 ways: first, physicians had to state if CKD was present and second, according to documented laboratory values eGFR or UACR. As per physician's assessment, 586 patients (14.5%) had a CKD. Identifying patients with

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

CKD by the documented values for eGFR or UACR at index date 1, resulted in 3175 PPS patients who were evaluable for this analysis. Number of patients with CKD (= having an eGFR of <60 ml/min and/or an UACR of >30 mg/g) increased to 886 (27.9%). Regarding patients per HCP specialty, cardiologists had the highest and diabetologists the lowest percentage of patients with CVD, 91.2% and 28.5%, respectively. Percentage of patients with CKD as assessed by the physician amounted to <20% for each HCP specialty. Identifying patients with CKD according to laboratory values, resulted in an increase by about 10% for each specialty.

<u>Secondary Outcome: Actual treatment use at study index date 1 in patients with and without established CVD) – (PPS)</u>

Established CV disease was defined as acute myocardial infarction (AMI), cardiology intervention (PCI or CABG) , ischemic heart disease (IHD), congestive heart failure (CHF), peripheral arterial disease (PAD), or stroke. Regarding patient distribution 'with' or 'without established CVD' according to T2D medication, more than 60% each of patients with 'Myocardial infarction', 'Cardiology intervention', and 'CHF - Confirmed by echocardiography' received empagliflozin. 48.9% of patients each with or without 'Peripheral arterial disease' received empagliflozin. Lowest percentage of patients irrespective of CVD had a prescription of GLP-1 RA. Analysis of T2D treatment according to CVD (yes/no) and HCP specialty showed that among patients with CVD enrolled by endocrinologists and diabetologists more than 50% received empagliflozin. Second frequently DPP4i was prescribed by these specialties. 75% of patients with CVD enrolled by cardiologists were treated with empagliflozin.

<u>Additional analysis: Actual treatment use at study index date 1 in patients with and without established CKD</u>

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

Among patients with CKD according to physician's assessment, the greatest percentage received DPP4i (49.3%). Taking into account patients with CKD identified by the documented laboratory values, 43.6% and 41.2% of these evaluable patients had a prescription of empagliflozin and DPP4i, respectively. Lowest percentage of patients with CKD irrespective of method of determination received prescription of GLP-1 RA.

<u>Secondary Outcome: Association of socioeconomic parameters with treatment decisions at index date 1 – (PPS)</u>

Generally, patients receiving GLP-1 RA had the highest percentage of employment (63.4%) and patients receiving DPP4i had the lowest percentage of employment (37.8%).

Generally, about 90% of patients in each medication group were statutory insured; however, patients with prescription of empagliflozin had the lowest percentage of statutory insurance and the highest percentage of private insurance compared to the other drugs. Endocrinologists had the highest percentage of privately insured T2D patients, with highest percentage among patients with first prescription of GLP-1 RA (14.6%) and lowest percentage among patients with first prescription of other SGLT2i (6.6%). Diabetologists had the lowest share of patients with private insurance, <0.5% in each treatment group. In all HCP specialties, share of privately insured patients was higher in empagliflozin medication group than in the other T2D treatment groups.

All socioeconomic factors were statistically significantly different distributed between T2D medication in patients enrolled by endocrinologists; this was true for employment and family status in patients enrolled by diabetologists, too. In contrast to this, no statistically significant differences regarding socioeconomic characteristics between T2D medication were observed in patients enrolled by cardiologists.

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

<u>Secondary outcome: Discontinuation rate, reasons for discontinuation and average duration of treatment for GLP-1 RA, DPP4i and SGLT2i after a follow up of approximately one year from the initial timepoint (= index date 2) – (FAS)</u>

361 patients (10.0%) of FAS discontinued the use of T2D medication which was prescribed at index date 1. Greatest and lowest share of patients with discontinuation of initial T2D treatment was observed for DPP4i (12.3%) and empagliflozin (7.9%), respectively. Among FAS patients treated by endocrinologists, highest percentage of discontinued patients was observed in GLP-1 RA treatment group (21.0%), whereas diabetologists had the highest share in DPP4i group (12.7%). Among FAS patients treated by cardiologists, only 8.3% of patients in empagliflozin treatment group discontinued initial therapy.

Predominant reasons, which were stated each for about one third of discontinued FAS patients, were ‘lack of efficacy’ and ‘financial burden regarding co-payment’, with 37.4% and 33.8%, respectively. 11.9% of patients discontinued initial T2D therapy due to adverse events. Analysis of reason according to participating countries revealed, that highest percentage of patients with ‘lack of efficacy’ and ‘financial burden regarding co-payment’ was reported by Czech Republic (71.1%) and Poland (55.8%), respectively. Endocrinologists selected for 42.0% of discontinued patients the reason ‘financial burden regarding co-payment’, whereas diabetologists terminated treatment of 41.8% of discontinued patients due to ‘lack of efficacy’. For 79.5% of patients with treatment discontinuation no other physician was involved in the decision to terminate the respective T2D therapy. Primarily involved physicians were ‘general practitioners’ (10.5%). Analysis according to specialty of treating physician reveals, that endocrinologists and diabetologists mainly involved other ‘endocrinologists’, 18.2% and 80.0%, respectively. Diabetologists made the decision to discontinue the T2D treatment for about 87% of their

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

discontinued patients alone. In case another physician's opinion was needed, primarily 'general practitioners' (10.8%) were asked.

Mean time to discontinuation amounted to 19.8 months. Analysis by T2D medication showed that for patients with GLP-1 RA prescription the highest mean time was calculated (20.6 months). For these patients, a median time to discontinuation of 23.3 months was estimated. For all other T2D medications median time was not reached. For patients receiving empagliflozin, DPP4i, and other SGLT2i, calculated mean time to T2D therapy discontinuation was 19.5 months, 18.3 months, and 14.0 months, respectively.

<u>Other analyses: Concomitant medications at study index date 1 – PPS</u>

Concomitant T2D medication as well as concomitant medication for CVD and CKD should be documented. For both types of medication, specified drug groups were listed and furthermore the use of 'other' drugs could be documented. For each patient, multiple concomitant medications could be selected.

Metformin was the most frequently used concomitant T2D medication irrespective of HCP specialty or modern T2D treatment, whereas pioglitazone and acarbose were the less frequently used concomitant T2D medication. Concomitant insulin was more frequently used by diabetologists than by endocrinologists or cardiologists.

Regarding concomitant CVD and CKD medications, patients of cardiologists received all specified concomitant medications more frequently than patients of endocrinologists or diabetologists. Most frequently 'antihypertensive ACE inhibitor or ARBs' were used irrespective of HCP specialty or modern T2D medication.

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**

Especially ‘low dose aspirin’ and ‘beta blockers’ were more frequently used by cardiologists than by endocrinologists or diabetologists.

<u>Other analyses: Comorbidities and T2D treatment by HCP specialties - PPS</u>

Cardiologists had the highest percentage of patients with each of the specified CVDs compared to endocrinologists or diabetologists. Greatest percentage of patients with about 60% of T2D patients treated by cardiologists had ‘ischemic heart disease’, which was recorded by about 34% and 20% of patients of endocrinologists and diabetologists, respectively.

Greatest percentage of patients with most of the specified CVDs were mainly treated with empagliflozin by endocrinologists and diabetologists, except for patients with peripheral arterial disease or stroke; slightly higher or nearly equal percentage of these patients were treated with DPP4i. Cardiologists prescribed empagliflozin mainly to patients with concomitant ischemic heart disease, myocardial infarction and peripheral arterial disease, whereas patients with congestive heart failure and stroke mainly received DPP4i. In case of cardiology intervention, cardiologists mostly used other SGLT2i as T2D therapy.

<u>Safety analysis: Adverse events / adverse reactions</u>

Within this observational study no adverse events (AE) had to be recorded in the eCRF. Only in case of discontinuation of T2D therapy due to adverse events, these had to be specified according to predefined categories. No severity or causality of the AE had to be recorded.

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**
	However, it was questioned, if the adverse event had to be reported according to section 11 of the study protocol [causal relationship to Jardiance®, Synjardy®, Trajenta®, or Jentadueto® (= Adverse Drug Reaction) or adverse event with fatal outcome or pregnancy]. A total of 361 patients discontinued their initial T2D therapy; for 43 patients (11.9%), occurrence of AE was stated as reason for discontinuation. Most of these patients reported 1 AE, 3 patients each experienced 2 AEs and 1 patient 4 AEs. 'Dysuria' was the most frequently recorded AE, it was reported by 11 patients (25.6%), followed by 'Balanitis and other genital infections' which was reported by 7 patients (16.3%), and 'Vulvovaginitis' and 'Urinary tract infection (including pyelonephritis and urosepsis)' reported by 5 patients each. Five AEs were assessed as related to the T2D medication Jardiance®, Synjardy®, Trajenta®, or Jentadueto® by the physician and thus were reported according to section 11 of the study protocol: Dyspepsia, abdominal pain, vulvovaginitis, increased urination and cerebrovascular event. Cerebrovascular event was assessed as serious adverse drug reaction. Outcome was 'recovered/resolved' for ADRs dyspepsia, abdominal pain, vulvovaginitis and increased urination, and 'recovered/resolved with sequelae' for SADR cerebrovascular event. Three patients were affected: one patient reported 3 non-serious ADRs and one patient each reported a non-serious and a serious ADR.		

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**
Discussion:	This observational study performed under routine conditions provided a good overview of characteristics of T2D patients in CEE countries. Five CEE countries with different political and economic situations participated and enrolled more than 4000 patients. T2D patients naïve to modern T2D treatment could be enrolled, thus patient characteristics and comorbidities as well as prescribed T2D medication is representative for CEE countries. Due to the great number of participating sites which were all medical practices only, a routine treatment in real-world non-hospital settings was depicted. As T2D is a multi-factorial disease with several risk factors and mutual influence on other diseases, e.g. CVDs, patients were not only treated by diabetologists, but also by endocrinologists and cardiologists. The physicians of each specialty followed their routine in treatment of their T2D patients. It could be seen, that diabetologists and cardiologists have similar reasons for choosing a specific T2D drug, whereas cardiologists laid a greater focus on CVDs. 91%, 86% and 64% of diabetologists, endocrinologists and cardiologists, respectively, did not involve another physician in the treatment decision, showing that especially cardiologists seek support when treating a disease for which they are not specialized. This is underlined by the fact that mainly endocrinologists and diabetologists were involved by cardiologists. The results of this NIS emphasized that in routine care guideline recommendations were not the primary reason for treatment decision. Especially the high percentage of missing laboratory values observed by all HCP specialties shows that these laboratory parameters are not routinely monitored. Although safety was not a part of the study design, in context with the discontinuation of the T2D treatment ADRs should be reported. No new safety signals were detected within this NIS.		

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Jardiance® 10 / 25 mg empagliflozin tablet Synjardy® 5 / 12.5 mg empagliflozin + 850 / 1,000 mg metformin tablet Trajenta® 5 mg linagliptin tablet Jentadueto® 2.5 mg linagliptin + 850 / 1,000 mg metformin tablet			
Name of active ingredient: empagliflozin (ATC: A10BK03) linagliptin (ATC: A10BH05)			
Report date: 24 Feb 2022	**Study number:** 1245-0187	**Version/Revision:** 1.0	**Version/Revision date:**
Marketing Authorisation Holder(s):	MAH: Boehringer Ingelheim International GmbH Binger Straße 173 55216 Ingelheim am Rhein, Germany This study was initiated, managed and sponsored by: Boehringer Ingelheim RCV GmbH & Co KG Division Medicine/Medical Affairs Dr. Boehringer-Gasse 5-11 A-1121 Wien, Austria		
Names and affiliations of principal investigators:	Co-ordinating investigator: Martin Prázný, MD, PhD, FRCP(Edin) associate professor 3rd Department of Internal Medicine, Diabetes center 1st Faculty of Medicine, Charles University and General Faculty Hospital in Prague, Czech Republic A “List of principal investigators” of the 177 participating centres is available as stand-alone document.		