Finerenone
(renal insufficiency, stage 1 and 2)

Addendum to Project A23-14
(dossier assessment)[1]

ADDENDUM

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Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

IQWiG employees involved in the addendum

- Isabelle Paulußen
- Florina Kerekes
- Philip Kranz
- Daniela Preukschat
- Christoph Schürmann

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List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AE	adverse event
CKD	chronic kidney disease
eGFR	estimated glomerular filtration rate
ESRD	end-stage renal disease
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
GLP-1	glucagon-like peptide 1
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
KDQOL-36	Kidney Disease Quality of Life Instrument-36
MCS	Mental Component Summary
MMRM	mixed-effects model repeated measures
PCS	Physical Component Summary
RCT	randomized controlled trial
SAE	serious adverse event
SGB	Sozialgesetzbuch (Social Code Book)
SGLT2	sodium-glucose cotransporter 2
VAS	visual analogue scale

1 Background

On 11 July 2023, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Project A23-14 (Finerenone – Benefit assessment according to § 35a Social Code Book V) [1].

The commission comprises the assessment of the data of the studies FIGARO-DKD and FIDELIO-DKD [2] presented in the dossier, taking into account the information from the commenting procedure [3,4].

The responsibility for the present assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

As explained in detail in dossier assessment A23-14 [1], the studies FIDELIO-DKD and FIGARO-DKD presented by the pharmaceutical company (hereinafter referred to as "the company") comparing finerenone versus the appropriate comparator therapy (ACT) were not included in the benefit assessment because the ACT in the sense of an optimized standard therapy was not implemented.

On the one hand, this was due to the fact that a large proportion of patients with pre-existing cardiovascular disease or at cardiovascular risk included in the subpopulation of the studies FIDELIO-DKD and FIGARO-DKD relevant for the benefit assessment (stage 1 and 2) were not treated with sodium-glucose cotransporter 2 (SGLT2) inhibitors or glucagon-like peptide 1 (GLP-1) receptor agonists according to the treatment algorithm of the current National Health Care Guideline (Nationale VersorgungsLeitlinie, NVL) for type 2 diabetes mellitus. In addition, optimized treatment of arterial hypertension was not guaranteed, especially for patients in the comparator arms of the two studies. Moreover, several drugs for the treatment of oedema or of heart failure that might occur in the course were not available. These points of criticism have not been resolved even after completion of the commenting procedure. Rather, it became clear from the oral hearing [5] that the use of SGLT2 inhibitors also represents the current health care standard of care in stage 1 and 2 chronic kidney disease (CKD) (i.e. not only in stages 3 and 4). This means that, according to the current health care standard, the patients included in the studies should have received an SGLT2 inhibitor not primarily only for their diabetes, but also for the treatment of their CKD. Therefore, the studies FIDELIO-DKD and FIGARO-DKD are still not rated as relevant for the benefit assessment.

However, the proportionally small subpopulation (9.8% received an SGLT2 inhibitor and 7.6% a GLP-1 receptor agonist at baseline) of patients who received concomitant treatment with SGLT2 inhibitors or GLP-1 receptor agonists from baseline is potentially relevant for the benefit assessment. However, the uncertainties described above regarding the optimized treatment of arterial hypertension as well as oedema or potentially occurring heart failure in the course also apply to this population. The company did not present the subgroup analyses on the use of SGLT2 inhibitors or GLP-1 receptor agonists at baseline (yes vs. no), which were pre-specified in the statistical analysis plan, in the dossier or in the comments [3], but submitted them subsequently to the oral hearing [4]. However, the subsequently submitted subgroup analyses are incomplete (data on health status and health-related quality of life are missing) and were consequently not used for the benefit assessment. There were therefore no suitable data for the benefit assessment. Results for selected benefit outcomes for the population of patients using SGLT2 inhibitors or GLP-1 receptor agonists at baseline are presented in Appendix B.

In the following, the studies FIDELIO-DKD and FIGARO-DKD are described in accordance with the commission, taking into account the information from the commenting procedure, and the results are presented.

2.1 Study characteristics

Detailed characteristics of the studies FIDELIO-DKD and FIGARO-DKD can be found in dossier assessment A23-14 [1]. The data on the course of the study not presented in dossier assessment A23-14 and the risk of bias across outcomes for both studies are described hereinafter.

Information on the course of the study

Table 1 shows the median and mean treatment durations of the patients and the median and mean observation periods for individual outcomes.

Table 1: Information on the course of the study – randomized controlled trial (RCT), direct comparison: finerenone vs. placebo

Study	FIDELIO-DKD		FIGARO-DKD	
duration of the study phase outcome category	finerenone	placebo	finerenone	placebo
Treatment duration [months][a]	N = 210[b]	N = 221[b]	N = 2326[b]	N = 2302[b]
Median [min; max]	34.3 [0.3; 50.4]	32.8 [0.6; 49.5]	35.8 [0.03; 61.0]	35.6 [0.2; 61.4]
Mean (SD)	32.6 (11.4)	31.0 (12.7)	35.7 (14.5)	35.4 (14.4)
Observation period [months][c]	N = 211	N = 221	N = 2327	N = 2304
Overall survival, morbidity, health-related quality of life, side effects[d]				
Median [min; max]	35.7 [1.4; 50.4]	36.0 [1.5; 49.5]	39.8 [1.0; 61.0]	39.4 [0.03; 61.6]
Mean (SD)	36.0 (8.4)	35.7 (9.2)	40.0 (11.8)	39.7 (12.0)

a. The treatment duration also includes the period of temporary treatment interruptions and is thus potentially overestimated.
b. The fact that few patients received no study medication results in a deviating number for the treatment duration.
c. Information on how the observation period was calculated is not available.
d. Only events that occurred during or up to 3 days after treatment interruption or discontinuation are included in the analyses of the side effect outcomes presented with the dossier. Information on observation durations is not available for the analyses subsequently submitted after the oral hearing, which address this problem but are incomplete (see Section 2.2.1).

max: maximum; min: minimum; N: number of analysed patients; RCT: randomized controlled trial; SD: standard deviation

The median treatment duration is slightly shorter in the FIDELIO-DKD study (34.3 months in the intervention arm and 32.8 months in the comparator arm) than in the FIGARO-DKD study (35.8 months in the intervention arm and 35.6 months in the comparator arm). The company

defined the duration of treatment as the time from the start of treatment until the definite termination of the study therapy. According to this definition, a treatment interruption in which no treatment with the study medication took place is also included in the calculation of the treatment duration. In Module 4 B, the company does not provide any information on how many patients interrupted a treatment and how long these interruptions lasted. The specified treatment durations are thus potentially clearly overestimated. It also remains unclear to what extent the duration of treatment differs between the study arms when periods of treatment interruption are not taken into account. The median observation duration is somewhat shorter in the FIDELIO-DKD study (35.7 months in the intervention arm and 36.0 months in the comparator arm) than in the FIGARO-DKD study (39.8 months in the intervention arm and 39.4 months in the comparator arm).

Risk of bias across outcomes (study level)

Table 2 shows the risk of bias across outcomes (risk of bias at study level).

Table 2: Risk of bias across outcomes (study level) – RCT, direct comparison: finerenone vs. placebo

Study	Adequate random sequence generation	Allocation concealment	Blinding		Nonselective reporting	No additional aspects	Risk of bias at study level
			Patients	Treatment providers			
FIDELIO-DKD	Yes	Yes	Yes	Yes	Yes	Yes	Low
FIGARO-DKD	Yes	Yes	Yes	Yes	Yes	Yes	Low
RCT: randomized controlled trial							

The risk of bias across outcomes was rated as low for both studies.

2.2 Results

2.2.1 Outcomes included

The following patient-relevant outcomes were to be included in the assessment:

- Mortality
  - all-cause mortality
- Morbidity
  - renal insufficiency (composite outcome)
  - cardiovascular morbidity/severe cardiovascular events

- health status, recorded using the visual analogue scale (VAS) of the EQ-5D

- Health-related quality of life
  - measured with the Kidney Disease Quality of Life Instrument (KDQOL)-36
- Side effects
  - serious adverse event (SAEs)
  - discontinuation due to adverse events (AEs)
  - hyperkalaemia (preferred term [PT], SAE)
  - further specific AEs, if any

The choice of patient-relevant outcomes deviates from that of the company, which used further outcomes in the dossier (Module 4 B).

Table 3 shows the outcomes for which data were available in the included study.

Table 3: Matrix of outcomes – RCT, direct comparison: finerenone versus placebo

Study	Outcomes									
	All-cause mortality	Renal insufficiency (composite outcome)[a]	Cardiovascular morbidity (composite outcome)	Severe cardiovascular events[b]	Health status (EQ-5D VAS)	Health-related quality of life (KDQOL-36)	SAEs	Discontinuation due to AEs	Hyperkalaemia (PT, SAEs)	Further specific AEs
FIDELIO-DKD	Yes	Yes	No[c]	No[d]	Yes	Yes	No[e]	No[e]	No[e]	No[e]
FIGARO-DKD	Yes	Yes	No[c]	No[d]	Yes	Yes	No[e]	No[e]	No[e]	No[e]

a. Renal insufficiency (defined as confirmed sustained decrease in eGFR to < 15 ml/min/1.73m^2 or ESRD [need for chronic dialysis treatment > 30 days unless it is apparent that dialysis treatment can be terminated after 90 days, or renal transplantation]).
b. Operationalized as cardiovascular hospitalization. This includes hospitalization for heart failure, other cardiovascular hospitalization (unstable angina pectoris, arrhythmias, peripheral arterial occlusive disease) or adjudicated cardiovascular event involving hospitalization (cardiovascular death, newly occurred atrial fibrillation or flutter, non-fatal myocardial infarction, non-fatal stroke, transient ischaemic attack).
c. No suitable data available; the composite cardiovascular outcome presented by the company, consisting of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and severe heart failure events (operationalized as hospitalization due to heart failure), is only presented as supplementary information; for reasons, see the following text section.
d. No suitable data available; for reasons, see the following text section.
e. No suitable analyses on superordinate AE outcomes available (see following text section); selection of specific AEs is therefore also not possible.

AE: adverse event; eGFR: estimated glomerular filtration rate; ESRD: end stage renal disease; KDQOL: Kidney Disease Quality of Life Instrument; PT: preferred term; RCT: randomized controlled trial; SAE: serious adverse event; VAS: visual analogue scale

Composite outcome on renal morbidity

The composite outcome of the studies on renal morbidity comprises the individual components of renal insufficiency (defined as confirmed sustained decrease in estimated glomerular filtration rate (eGFR) to < 15 ml/min/1.73m^2 or end-stage renal disease (ESRD) [need for chronic dialysis treatment > 30 days unless it is apparent that dialysis treatment can be terminated after 90 days, or renal transplantation]), eGFR reduction ≥ 57% and renal death. Due to the high mean eGFR baseline values (approx. 80 ml/min/1.73m^2) of the patients, sufficient patient relevance of the component “eGFR decrease ≥ 57%” cannot be assumed in the present data situation. Consequently, the composite outcome is not used as a suitable

analysis in the context of this addendum, but is merely presented as supplementary information.

Renal insufficiency (component of the composite outcome of renal morbidity)

In Module 4 B, the company presents analyses on the outcome of renal insufficiency, consisting of the components ESRD and a sustained decrease in eGFR to < 15 ml/min/1.73m². Dossier assessment A23-15 describes that the definition of the component ESRD in the study documents deviates from the one provided in to Module 4 A [6].

In its comments, the company states that the definitions and criteria for the identification of events for renal and cardiovascular outcomes described in Module 4 A and Module 4 B correspond to the specifications determined a priori for the FIDELIO-DKD and FIGARO-DKD studies, which are described in detail in the Clinical Event Committee Charter across studies [7].

The analyses on the outcome of renal insufficiency are used as sufficiently suitable analyses in this addendum.

Cardiovascular morbidity/severe cardiovascular events

The composite outcome of the studies on cardiovascular morbidity includes the individual components of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and severe heart failure events (operationalized as hospitalization due to heart failure). However, the analyses do not include hospitalizations for other cardiovascular reasons (e.g. hospitalization due to atrial fibrillation, unstable angina pectoris or arrhythmias), which, for example, occurred more than twice as often as hospitalizations due to heart failure in the FIGARO-DKD study. The composite outcome on cardiovascular morbidity thus covers only part of the relevant cardiovascular events.

In its comments, the company subsequently submitted analyses for cardiovascular hospitalization that are basically suitable for depicting severe cardiovascular events. However, these analyses are incomplete (results for the individual studies are lacking, and there is no information for the relevant subpopulations on how the included events are distributed among the different components [e.g. cardiovascular mortality, transient ischaemic attack, other cardiovascular hospitalizations]).

Overall, the results of the composite outcome “cardiovascular morbidity” as well as of severe cardiovascular events, operationalized as cardiovascular hospitalization, are only presented as supplementary information in this addendum due to the shortcomings described.

Other morbidity outcomes

The composite outcome of renal morbidity, consisting of the individual components "renal insufficiency", "renal death" and "eGFR decrease ≥ 40%", the outcome of confirmed deterioration of CKD to stage 4 or 5, and total hospitalization are each presented as supplementary information in Appendix A.

Health status (EQ-5D VAS) and health-related quality of life (KDQOL-36)

For the outcomes of health status (recorded with the EQ-5D VAS) and health-related quality of life (recorded with the KDQOL-36), the company presented responder analyses on deterioration and improvement, respectively, with the response criterion 15% of the scale range (EQ-5D VAS: 15 points; KDQOL-36: F [PCS]) = 8 points; Mental Component Summary [MCS] = 9 points; burden of the kidney disease, symptoms and problems of kidney disease and effects of kidney disease on daily life 15 points each). Although the response criteria used correspond to the specifications of the General Methods 6.1 of the Institute [8], the company calculates the relative risk for deterioration or improvement compared to baseline over the entire documentation period and not at a defined time point of documentation, e.g. at month 24. A patient is thus considered a responder in the analyses of the company if he/she showed deterioration or improvement at (any) time point in the course of the study. This analysis is not informative because the time of deterioration or improvement is not taken into account in the analyses submitted by the company. The mixed-effects model repeated measures (MMRM) analyses submitted by the company are therefore used for this addendum.

SAEs, discontinuation due to AEs, hyperkalaemia (PT, SAE) and specific AEs

In the studies FIDELIO-DKD and FIGARO-DKD, AEs were recorded over the entire observation period, regardless of whether the patients were still receiving treatment with the study medication. However, only events that occurred during treatment with the study medication and up to 3 days after a treatment interruption or treatment discontinuation were included in the analyses on AEs, SAEs and discontinuation due to AEs submitted by the company. The company provided no data on the proportion of patients with treatment interruption (> 3 days) and the corresponding duration of the interruption. In the total population of the FIDELIO-DKD study, a proportion of 53.6% in the intervention arm and 45.0% in the comparator arm interrupted treatment; in the total population of the FIGARO-DKD study, a proportion of 50.3% in the intervention arm and 47.4% in the comparator arm interrupted treatment [6]. This proportion is not expected to differ in the subpopulation relevant to this addendum. AEs that occurred during a treatment interruption of more than 3 days are therefore not included in the analyses for a relevant proportion of patients. Likewise, patients who discontinued treatment with the study medication (22-24% in the FIDELIO-DKD study and 24-26% in the FIGARO-DKD study, see dossier assessment A23-14 [1] are not included in the analyses with their entire observation period. This approach is not appropriate. In principle,

analyses that include all events in the observation period are necessary for the benefit assessment.

The company subsequently submitted data with its comment in which, according to its information, all AEs up to 30 days after the last intake of the study medication are taken into account. However, effect estimates and p-values are only available for the overall rate of SAEs; data on discontinuation due to AEs and specific AEs are completely missing. The subsequently submitted data are therefore incomplete.

Therefore, no suitable data are available for the outcomes of SAEs, discontinuation due to AEs, hyperkalaemia (PT, SAE) and other specific AEs. The results of the - unsuitable - data submitted with the dossier (AEs that occurred up to 3 days after treatment interruption or discontinuation) are presented as supplementary information in Appendix A

2.2.2 Risk of bias

Table 4 describes the risk of bias for the results of the considered outcomes.

Table 4: Risk of bias across outcomes and outcome-specific risk of bias – RCT, direct comparison: finerenone versus placebo

Study	Study level	Outcomes									
		All-cause mortality	Renal insufficiency[a]	Cardiovascular morbidity (composite outcome)	Severe cardiovascular events[b]	Health status (EQ-5D VAS)	Health-related quality of life (KDQOL-36)	SAEs	Discontinuation due to AEs	Hyperkalaemia (PT, SAEs)	Further specific AEs
FIDELIO-DKD	L	L	L	–[c]	–[d]	H[e]	H[e]	–[f]	–[f]	–[f]	–[f]
FIGARO-DKD	L	L	L	–[c]	–[d]	H[e]	H[e]	–[f]	–[f]	–[f]	–[f]

a. Renal insufficiency (defined as confirmed sustained decrease in eGFR to < 15 ml/min/1.73m^2 or ESRD [need for chronic dialysis treatment > 30 days unless it is apparent that dialysis treatment can be terminated after 90 days, or renal transplantation]).
b. Operationalized as cardiovascular hospitalization.
c. No suitable data available (see Section 2.2.1); the composite cardiovascular outcome presented by the company, consisting of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and severe heart failure events (operationalized as hospitalization due to heart failure), is only presented as supplementary information.
d. No suitable data (see Section 2.2.1).
e. Decreasing questionnaire response rate over the course of the study.
f. No suitable analyses on superordinate AE outcomes available (see Section 2.2.1); selection of specific AEs is therefore also not possible.

AE: adverse event; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; KDQOL: Kidney Disease Quality of Life Instrument; PT: Preferred Term; RCT: randomized controlled trial; SAE: serious adverse event; VAS: visual analogue scale

The risk of bias for the results of the outcomes on all-cause mortality and renal insufficiency was rated as low. The results of the outcomes on health status, recorded using the EQ-5D VAS, and on health-related quality of life, recorded with the KDQOL-36, show a high risk of bias due to decreasing questionnaire response rates over the course of the study. No suitable data are available for the outcomes on cardiovascular morbidity (as well as on serious cardiovascular events) and side effects (for reasons, see Section 2.2.1).

2.2.3 Results

Table 5 and Table 6 summarize the results comparing finerenone with placebo in adult patients with stage 1 and 2 CKD with albuminuria associated with type 2 diabetes mellitus. Outcomes on renal morbidity with eGFR decline ≥ 40%, on confirmed worsening of CKD to stage 4 or 5, total hospitalization and data on side effects are presented as supplementary

information in Appendix A of the full dossier assessment and outcomes for the subpopulation with concomitant treatment of SGLT2 inhibitors or GLP-1 receptor agonists at baseline are presented in Appendix B of the full dossier assessment. Where necessary, calculations conducted by the Institute are provided in addition to the data from the company's dossier. The Kaplan-Meier curves on the event time analyses of the outcomes are presented in I Appendix C of the full dossier assessment.

Table 5: Results (mortality, morbidity, time to event) – RCT, direct comparison: finerenone vs. placebo (multipage table)

Outcome category outcome study	Finerenone N	Finerenone median time to event in months [95% CI] patients with event n (%)	Placebo N	Placebo median time to event in months [95% CI] patients with event n (%)	Finerenone vs. placebo HR [95% CI]; p-value[a]
Mortality					
All-cause mortality					
FIDELIO-DKD	211	NA 17 (8.1)	221	NA 14 (6.3)	1.28 [0.63; 2.60]; 0.490
FIGARO-DKD	2327	NA 166 (7.1)	2304	NA 211 (9.2)	0.77 [0.63; 0.95]; 0.013
Total[b]					0.80 [0.66; 0.98]; 0.029
Morbidity					
Renal morbidity					
Renal morbidity with eGFR decrease ≥ 57% (composite outcome) (provided as supplementary information)					
FIDELIO-DKD	*211*	*NA* *7 (3.3)*	*221*	*NA* *16 (7.2)*	*0.43 [0.18; 1.05];* *0.056*
FIGARO-DKD	*2327*	*61.90 [NC]* *73 (3.1)*	*2304*	*NA* *108 (4.7)*	*0.66 [0.49; 0.89];* *0.006*
Total[b]					*0.63 [0.48; 0.84];* *0.001*
Renal insufficiency[c, d]					
FIDELIO-DKD	211	NA 2 (0.9)	221	NA 8 (3.6)	0.25 [0.05; 1.20]; 0.062
FIGARO-DKD	2327	NA 22 (0.9)	2304	NA 38 (1.6)	0.57 [0.34; 0.96]; 0.032
Total[b]					0.52 [0.32; 0.85]; 0.008
Sustained decrease in eGFR to < 15 ml/min/1.73 m² [c]					
FIDELIO-DKD	211	NA 1 (0.5)	221	NA 6 (2.7)	0.17 [0.02; 1.43]; 0.064
FIGARO-DKD	2327	NA 12 (0.5)	2304	NA 21 (0.9)	0.56 [0.27; 1.13]; 0.102
Total[b]					0.48 [0.25; 0.93]; 0.026
ESRD[c,e]					
FIDELIO-DKD	211	NA 1 (0.5)	221	NA 5 (2.3)	0.21 [0.02; 1.81]; 0.118
FIGARO-DKD	2327	NA 17 (0.7)	2304	NA 34 (1.5)	0.49 [0.27; 0.87]; 0.013

Table 5: Results (mortality, morbidity, time to event) – RCT, direct comparison: finerenone vs. placebo (multipage table)

Outcome category outcome study	Finerenone N	Finerenone median time to event in months [95% CI] patients with event n (%)	Placebo N	Placebo median time to event in months [95% CI] patients with event n (%)	Finerenone vs. placebo HR [95% CI]; p-value[a]
Total[b]					0.46 [0.26; 0.80]; 0.005
eGFR decline by ≥ 57%[c] (supplementary information)					
FIDELIO-DKD	*211*	*NA* *6 (2.8)*	*221*	*NA* *16 (7.2)*	*0.37 [0.14; 0.95]; 0.031*
FIGARO-DKD	*2327*	*NA* *69 (3.0)*	*2304*	*NA* *97 (4.2)*	*0.70 [0.51; 0.95]; 0.021*
Total[b]					*0.65 [0.48; 0.87]; 0.004*
Renal death[c] (supplementary information)					
FIDELIO-DKD	*211*	*NA* *0 (0)*	*221*	*NA* *0 (0)*	*NC*
FIGARO-DKD	*2327*	*NA* *0 (0)*	*2304*	*NA* *1 (< 0.1)*	*0.00 [0.00; ND]; 0.365*
Total[b]					–
Cardiovascular morbidity	No suitable data				
Cardiovascular morbidity (composite outcome) (supplementary information)					
FIDELIO-DKD	*211*	NA 34 (16.1)	*221*	NA 33 (14.9)	*1.08 [0.67; 1.75]; 0.740*
FIGARO-DKD	*2327*	NA 263 (11.3)	*2304*	NA 291 (12.6)	*0.89 [0.75; 1.05]; 0.169*
Total[b]					*0.91 [0.78; 1.06]; 0.238*
Cardiovascular death[c]					
FIDELIO-DKD	*211*	*NA* *13 (6.2)*	*221*	*NA* *12 (5.4)*	*1.15 [0.52; 2.52]; 0.729*
FIGARO-DKD	*2327*	NA 105 (4.5)	*2304*	NA 124 (5.4)	*0.83 [0.64; 1.08]; 0.166*
Total[b]					*0.86 [0.67; 1.10]; 0.225*
Non-fatal myocardial infarction[c]					
FIDELIO-DKD	*211*	*NA* *8 (3.8)*	*221*	*NA* *9 (4.1)*	*0.93 [0.36; 2.41]; 0.876*
FIGARO-DKD	*2327*	*NA* *55 (2.4)*	*2304*	*NA* *49 (2.1)*	*1.11 [0.75; 1.63]; 0.599*
Total[b]					*1.10 [0.77; 1.57]; 0.608*

Table 5: Results (mortality, morbidity, time to event) – RCT, direct comparison: finerenone vs. placebo (multipage table)

Outcome category **outcome** **study**	**Finerenone** **N**	**median time to event in months [95% CI]** **patients with event n (%)**	**Placebo** **N**	**median time to event in months [95% CI]** **patients with event n (%)**	**Finerenone vs. placebo** **HR [95% CI]; p-value[a]**
Non-fatal stroke[c]					
FIDELIO-DKD	*211*	*NA* *8 (3.8)*	*221*	*NA* *11 (5.0)*	*0.77 [0.31; 1.91]; 0.572*
FIGARO-DKD	*2327*	*NA* *76 (3.3)*	*2304*	*NA* *65 (2.8)*	*1.15 [0.83; 1.61]; 0.400*
Total[b]					*1.11 [0.81; 1.51]; 0.514*
Severe heart failure events (operationalized as hospitalization for heart failure)[c]					
FIDELIO-DKD	*211*	*NA* *9 (4.3)*	*221*	*NA* *13 (5.9)*	*0.72 [0.31; 1.68]; 0.442*
FIGARO-DKD	*2327*	*NA* *59 (2.5)*	*2304*	*NA* *91 (3.9)*	*0.64 [0.46; 0.89]; 0.008*
Total[b]					*0.65 [0.48; 0.88]; 0.005*
Severe cardiovascular events (presented as supplementary information)[g]					
FIDELIO-DKD	*211*	*ND[h]*	*221*	*ND[h]*	*ND*
FIGARO-DKD	*2327*	*ND[h]*	*2304*	*ND[h]*	*ND*
Total[d]					*0.99 [0.86; 1.13]; 0.839*
Side effects	No suitable data				

Table 5: Results (mortality, morbidity, time to event) – RCT, direct comparison: finerenone vs. placebo (multipage table)

Outcome category outcome study	Finerenone N	Finerenone median time to event in months [95% CI] patients with event n (%)	Placebo N	Placebo median time to event in months [95% CI] patients with event n (%)	Finerenone vs. placebo HR [95% CI]; p-value[a]

a. For the individual studies, HR [95% CI] from Cox regression model, stratified by region, and for the FIGARO-DKD study additionally by urine albumin-creatinine ratio (UACR) at the time of screening and cardiovascular history; p-value: log-rank test, stratified by the same factors.
b. Calculation from IPD meta-analysis with factor study as fixed effect (for model see footnote "a"); stratified by region, UACR at time of screening and cardiovascular history.
c. The presentation of the individual components does not comprise the qualifying events, but all events that occurred during the course of the study.
d. Renal insufficiency was defined as the occurrence of ESRD or an eGFR < 15 ml/min/1.73m², confirmed by a 2nd measurement ≥ 4 weeks after the 1st measurement.
e. According to Module 4 B, ESRD was defined as:

- Kidney transplant
- Peritoneal dialysis or haemodialysis required for at least 30 days and for which it is not apparent that treatment can be stopped after 90 days.
- acute kidney injury resulting in dialysis or death and occurring during dialysis treatment
- Renal replacement therapy indicated for symptomatic uraemia (eGFR of < 15 ml/min/1.73m^2 for at least 30 days) or asymptomatic uraemia (eGFR of < 8 ml/min/1.73m^2) but not available or accessible, refused or considered futile; ESRD is then diagnosed even without initiation of renal replacement therapy.

f. A death was classified as renal death if the patient died and had not received clinically indicated renal replacement therapy and there is no other probable cause of death.
g. Composite outcome, consisting of hospitalization for heart failure, other cardiovascular hospitalization (unstable angina pectoris, arrhythmias, peripheral arterial occlusive disease) or adjudicated cardiovascular event involving hospitalization (cardiovascular death, newly occurred atrial fibrillation or flutter, non-fatal myocardial infarction, non-fatal stroke, transient ischaemic attack).
h. In the IPD meta-analysis, 428 (16.9%) patients in the intervention arm and 430 (17.0%) patients in the comparator arm had an event.

CI: confidence interval; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; HR: hazard ratio; IPD: individual patient data; n: number of patients with (at least 1) event; N: number of analysed patients; NA: not achieved; NC: not calculable; RCT: randomized controlled trial; UACR: urine albumin creatinine ratio

Table 6: Results (morbidity, health-related quality of life, continuous) – RCT, direct comparison: finerenone versus placebo (multipage table)

Study outcome category outcome	Finerenone			Placebo			Finerenone vs. placebo
	N[a]	values at baseline mean (SD)	mean change in the course of the study mean[b] (95% CI)	N[a]	values at baseline mean (SD)	mean change in the course of the study mean[b] (95% CI)	MD [95% CI]; p-value[b]
Morbidity							
Health status (EQ-5D VAS)[c]							
FIDELIO-DKD	194	74.6 (16.2)	0.12 [-2.22; 2.45]	205	75.0 (16.5)	0.04 [-2.10; 2.19]	0.07 [-2.28; 2.43]; 0.952
FIGARO-DKD	2151	73.1 (16.9)	0.43 [-0.26; 1.12]	2133	74.4 (16.5)	0.41 [-0.30; 1.12]	0.02 [-0.72; 0.77]; 0.956
Total[d]							0.10 [-0.57; 0.77]; 0.766
Health-related quality of life							
KDQOL-36[e]							
PCS							
FIDELIO-DKD	193	43.4 (9.9)	-0.44 [-1.68; 0.81]	202	43.6 (9.9)	-2.24 [-3.59; -0.89]	1.80 [0.37; 3.24]; 0.014
FIGARO-DKD	2137	43.4 (9.8)	-1.25 [-1.66; -0.84]	2122	43.7 (9.8)	-1.24 [-1.66; -0.82]	-0.01 [-0.45; 0.43]; 0.964
Total[d]							0.13 [-0.26; 0.52]; 0.509
MCS							
FIDELIO-DKD	193	51.3 (9.4)	-0.28 [-1.67; 1.12]	202	52.8 (9.3)	-1.37 [-2.72; -0.01]	1.09 [-0.36; 2.55]; 0.141
FIGARO-DKD	2137	50.8 (10.0)	-0.37 [-0.81; 0.06]	2122	51.0 (9.8)	-0.32 [-0.76; 0.13]	-0.06 [-0.53; 0.41]; 0.804
Total[d]							0.04 [-0.38; 0.46]; 0.855
Disease burden of kidney disease							
FIDELIO-DKD	194	75.2 (25.9)	4.24 [1.11; 7.37]	205	76.2 (25.1)	2.88 [-0.49; 6.24]	1.37 [-2.05; 4.78]; 0.432
FIGARO-DKD	2148	75.4 (26.2)	1.47 [0.38; 2.55]	2128	76.1 (25.1)	0.95 [-0.15; 2.05]	0.51 [-0.63; 1.66]; 0.381
Total[d]							0.60 [-0.49; 1.68]; 0.281[f]
Symptoms and problems of kidney disease							
FIDELIO-DKD	194	82.6 (15.4)	-0.19 [-1.82; 1.45]	205	84.5 (13.6)	-2.25 [-3.97; -0.53]	2.06 [0.24; 3.88]; 0.027
FIGARO-DKD	2151	83.1 (15.6)	-1.01 [-1.61; -0.42]	2133	83.9 (15.0)	-1.04 [-1.63; -0.44]	0.02 [-0.61; 0.65]; 0.944

Table 6: Results (morbidity, health-related quality of life, continuous) – RCT, direct comparison: finerenone versus placebo (multipage table)

Study outcome category / outcome	Finerenone N[a]	Finerenone values at baseline mean (SD)	Finerenone mean change in the course of the study mean[b] (95% CI)	Placebo N[a]	Placebo values at baseline mean (SD)	Placebo mean change in the course of the study mean[b] (95% CI)	Finerenone vs. placebo MD [95% CI]; p-value[b]
Total[d]							0.16 [-0.41; 0.73]; 0.586
Effects of kidney disease on everyday life							
FIDELIO-DKD	194	87.5 (14.5)	0.62 [-1.11; 2.34]	205	88.7 (14.3)	-1.72 [-3.62; 0.18]	2.34 [0.36; 4.31]; 0.021
FIGARO-DKD	2143	87.2 (15.9)	0.46 [-0.18; 1.10]	2128	87.4 (15.4)	-0.05 [-0.72; 0.61]	0.52 [-0.17; 1.20]; 0.139
Total[d]							0.34 [-0.28; 0.96]; 0.288

a. Number of patients taken into account in the analysis for calculating the effect estimation; baseline values may rest on different patient numbers.
b. Individual studies: MMRM with the covariates treatment group, region and, for the FIGARO-DKD study, additionally the covariates UACR at the time of screening (as a categorical variable) and history of cardiovascular disease, time, interaction from treatment and time, baseline value and interaction from baseline value and time.
d. Higher (increasing) values indicate improved symptoms; positive effects (intervention minus control) indicate an advantage for the intervention (scale range 0 to 100).
d. IPD meta-analysis: MMRM with the covariates study, treatment group, region, UACR at time of screening, history of cardiovascular disease, time, interaction from treatment and time, baseline value and interaction from baseline value and time.
e. Higher (increasing) values mean improved symptoms/health-related quality of life; positive effects (intervention minus control) mean an advantage for the intervention (scale range: Physical Component Summary (PCS) 13 to 69 points; Mental Component Summary (MCS) 10 to 70 points; disease burden of kidney disease, symptoms and problems of kidney disease, and effects of kidney disease on everyday life 0 to 100 points each).
f. Institute's calculation from aggregated data, fixed-effect model. According to the company, no results are available due to convergence problems.

CI: confidence interval; eGFR: estimated glomerular filtration rate; IPD: individual patient data; KDQOL: Kidney Disease Quality Of Life; MCS: Mental Component Summary; MD: mean difference; MMRM: mixed-effects model repeated measures; N: number of analysed patients; PCS: Physical Component Summary; RCT: randomized controlled trial; SD: standard deviation; UACR: urine albumin creatinine ratio; VAS: visual analogue scale

Mortality

All-cause mortality

For the outcome of all-cause mortality, the meta-analysis of the studies FIDELIO-DKD and FIGARO-DKD showed a statistically significant difference in favour of finerenone over placebo.

Morbidity

Renal insufficiency

For the outcome of renal insufficiency, the meta-analysis of the studies FIDELIO-DKD and FIGARO-DKD showed a statistically significant difference in favour of finerenone over placebo.

Cardiovascular morbidity (composite outcome) and severe cardiovascular events (operationalized as cardiovascular hospitalization)

No suitable data are available for the composite outcome of cardiovascular morbidity and severe cardiovascular events (operationalized as cardiovascular hospitalization).

Health status (EQ-5D VAS) analysed using MMRM

For the outcome of health status (recorded via the EQ-5D VAS), the meta-analysis of the studies FIDELIO-DKD and FIGARO-DKD does not show any statistically significant difference between the treatment groups.

Health-related quality of life

KDQOL-36 analysed using MMRM

PCS, MCS, disease burden of kidney disease, symptoms and problems of kidney disease and impact of kidney disease on everyday life

For each of the 5 domains of the KDQOL-36, i.e. PCS, MCS, burden of kidney disease, symptoms and problems of kidney disease and impact of kidney disease on everyday life, the meta-analysis of the studies FIDELIO-DKD and FIGARO-DKD showed no statistically significant difference between the treatment groups.

Side effects

No suitable data are available for outcomes of the category of side effects.

2.2.4 Subgroups and other effect modifiers

The following subgroup characteristics are relevant for the present analysis:

- Age (< 65 years versus ≥ 65 years)
- Sex (male versus female)
- Region (Europe vs. North America vs. Asia vs. Latin America vs. other)
- Albuminuria at screening visit (high albuminuria vs. very high albuminuria)

Interaction tests are performed when at least 10 patients per subgroup are included in the analysis. Moreover, for binary data, there had to be at least 10 events in at least 1 subgroup.

Only the results with an effect modification with a statistically significant interaction between treatment and subgroup characteristic (p-value < 0.05) are presented. In addition, subgroup results are presented only if there is a statistically significant and relevant effect in at least one subgroup.

Using the methods described above, the available subgroup results do not reveal any effect modifications.

2.2.5 Summary of the results

Overall, the meta-analysis shows advantages of finerenone for the outcome of all-cause mortality and the outcome of renal insufficiency. Suitable data for cardiovascular morbidity and side effects are lacking.

2.3 Summary

The data subsequently submitted by the company in the commenting procedure have not changed the conclusion on the added benefit of finerenone from dossier assessment A23-14.

The following Table 7 shows the result of the benefit assessment of finerenone under consideration of dossier assessment A23-14 and the present addendum.

Table 7: Finerenone – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adults with CKD (stage 1 and 2 with albuminuria) associated with type 2 *diabetes mellitus	Optimized standard therapy for the treatment of CKD and type 2 diabetes mellitus, taking into account the underlying disease(s) and common comorbidities (such as dyslipoproteinaemia, hypertension, anaemia)	Added benefit not proven
a. Presented is the ACT specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The G-BA decides on the added benefit.

3 References

The reference list contains citations provided by the company in which bibliographical information may be missing.

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2. Bayer Vital. Finerenon (KERENDIA); Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 2023 [Accessed: 28.06.2023]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/927/#dossier.

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6. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Finerenon (Niereninsuffizienz, Stadium 3 und 4); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2023 [Accessed: 13.06.2023]. URL: https://www.iqwig.de/download/a23-15_finerenon_nutzenbewertung-35a-sgb-v_v1-0.pdf.

7. Aci Clinical. CEC Charter 2019: Finerenone (BAY 94-8862) Phase III Program Clinical Event Committee Charter, Version 3.0.

8. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 6.1 [online]. 2022 [Accessed: 27.01.2022]. URL: https://www.iqwig.de/methoden/allgemeine-methoden-v6-1.pdf.

Appendix A Supplementary presentation of results on morbidity and side effects

Table 8: Supplementary presentation of results (morbidity, time to event) – RCT, direct comparison: finerenone vs. placebo

Study outcome category outcome	Finerenone N	Finerenone median time to event in months [95% CI] patients with event n (%)	Placebo N	Placebo median time to event in months [95% CI] patients with event n (%)	Finerenone vs. placebo HR [95% CI]; p-value[a]
Morbidity					
Renal morbidity with eGFR decrease ≥ 40% (composite outcome) (provided as supplementary information)[b, c]					
FIDELIO-DKD	*211*	*NA* *34 (16.1)*	*221*	*NA* *36 (16.3)*	*0.98 [0.61; 1.56]; 0.919*
FIGARO-DKD	*2327*	*NA* *217 (9.3)*	*2304*	*NA* *281 (12.2)*	*0.75 [0.63; 0.90]; 0.002*
Total[d]					*0.78 [0.66; 0.92]; 0.003*
Confirmed deterioration of CKD to stage 4 or 5 (supplementary information)[e]					
FIDELIO-DKD	*211*	*NA* *11 (5.2)*	*221*	*NA* *18 (8.1)*	*0.62 [0.29; 1.31]; 0.204*
FIGARO-DKD	*2327*	*NA* *56 (2.4)*	*2304*	*NA* *79 (3.4)*	*0.69 [0.49; 0.97]; 0.031*
Total[d]					*0.67 [0.49; 0.91]; 0.011*
Total hospitalization (supplementary information)					
FIDELIO-DKD	*211*	*47.43 [NC]* *87 (41.2)*	*221*	*45.83 [NC]* *94 (42.5)*	*0.94 [0.70; 1.26]; 0.662*
FIGARO-DKD	*2327*	*NA* *903 (38.8)*	*2304*	*57.10 [NC]* *918 (39.8)*	*0.97 [0.88; 1.06]; 0.506*
Total[d]					*0.97 [0.78; 1.20]; 0.758*

a. Individual studies: HR [95% CI] from Cox regression model, stratified by region, and for the FIGARO-DKD study additionally by UACR at the time of screening and cardiovascular history; p-value: log-rank test, stratified by the same factors.
b. Composite outcome, consisting of renal insufficiency, sustained decrease in eGFR by ≥ 40% from baseline, with the decrease lasting at least 4 weeks, and renal death.
c. Data for the single component of sustained decrease in eGFR by ≥ 40% from baseline are not available. For results on the individual components of renal failure and renal death, see renal morbidity with a decrease in eGFR ≥ 57% (Table 5).
d. IPD meta-analysis: HR [95% CI] from Cox regression model, stratified by region, UACR at the time of screening and cardiovascular history; p-value: log-rank test, stratified by the same factors.
e. Decrease in eGFR by ≥ 25% to < 30 ml/min/1.73m^2 or to < 15 ml/min/1.73m^{2}compared to baseline, which had to be confirmed in a 2nd measurement ≥ 4 weeks after the 1st measurement.

CI: confidence interval; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; HR: hazard ratio; IPD: individual patient data; n: number of patients with (at least 1) event; N: number of analysed patients; NA: not achieved; NC: not calculable; RCT: randomized controlled trial; UACR: urine albumin creatinine ratio

Table 9: Results (side effects, dichotomous) – RCT, direct comparison: finerenone vs. placebo

Study outcome category outcome	Finerenone N	Finerenone patients with event n (%)	Placebo N	Placebo patients with event n (%)	Finerenone vs. placebo RR [95% CI]; p-value[a]
Side effects					
AEs (supplementary information)[b, c]					
FIDELIO-DKD	*210*	*176 (83.8)*	*221*	*177 (80.1)*	*–*
FIGARO-DKD	*2326*	*1926 (82.8)*	*2302*	*1924 (83.6)*	*–*
SAEs (supplementary information)[b, c]					
FIDELIO-DKD	*210*	*64 (30.5)*	*221*	*65 (29.4)*	*1.04 [0.78; 1.38]; 0.809*
FIGARO-DKD	*2326*	*661 (28.4)*	*2302*	*696 (30.2)*	*0.94 [0.86; 1.03]; 0.175*
Total[d]					*0.95 [0.87; 1.03]; 0.221*
Discontinuation due to AEs (supplementary information)[b]					
FIDELIO-DKD	*210*	*10 (4.8)*	*221*	*11 (5.0)*	*0.96 [0.42; 2.21]; 0.917*
FIGARO-DKD	*2326*	*85 (3.7)*	*2302*	*94 (4.1)*	*0.90 [0.67; 1.19]; 0.449*
Total[d]					*0.90 [0.69; 1.18]; 0.454*
Hyperkalaemia (PT, SAE) (supplementary information)[b]					
FIDELIO-DKD	*210*	*ND*	*221*	*ND*	*ND*
FIGARO-DKD	*2326*	*ND*	*2302*	*ND*	*ND*
Total[d]					*ND*

a. Individual studies: log-binomial regression model.
b. No meaningfully interpretable data available. However, only events that occurred during treatment with the study medication and up to 3 days after a treatment interruption or treatment discontinuation were included in the analyses. This is a relevant problem in the present data situation, as in the total population of the FIDELIO-DKD study a proportion of 53.6% in the intervention arm and 45.0% in the comparator arm, and in the total population of the FIGARO-DKD study 50.3% in the intervention arm and 47.4% in the comparison arm interrupted treatment (no data for the relevant subpopulation). Likewise, patients who discontinued treatment with the study medication (22-24% in the FIDELIO-DKD study and 24-26% in the FIGARO-DKD study, see dossier assessment A23-14 [1] are not included in the analyses with their entire observation period.
c. Excluding disease-related events.
d. IPD meta-analysis: log-binomial regression model with study as covariate.

AE: adverse event; CI: confidence interval; IPD: individual patient data; n: number of patients with (at least one) event; N: number of analysed patients; ND: no data; PT: Preferred Term; RCT: randomized controlled trial; RR: relative risk; SAE: serious adverse event; UACR: urine albumin creatinine ratio

Appendix B Supplementary presentation of results of the subpopulation with concomitant treatment of SGLT-2 inhibitors or GLP-1 receptor agonists at baseline

Table 10: Results (mortality, morbidity, time to event) - RCT, direct comparison: finerenone + optimized standard therapy vs. placebo + optimized standard therapy, population with concomitant treatment with SGLT2 inhibitors or GLP-1 receptor agonists at baseline (multipage table)

Outcome category **outcome** **study**	**Finerenone + optimized standard therapy**		**Placebo + optimized standard therapy**		**Finerenone + optimized standard therapy vs. placebo + optimized standard therapy**
	N	**median time to event in months [95% CI]** **patients with event n (%)**	**N**	**median time to event in months [95% CI]** **patients with event n (%)**	**HR [95% CI]; p-value[a]**
Mortality					
Overall survival					
FIDELIO-DKD	ND	ND	ND	ND	ND
FIGARO-DKD	ND	ND	ND	ND	ND
Total	413	ND 18 (4.4)	374	ND 20 (5.3)	0.68 [0.35; 1.32]; 0.252
Morbidity					
Renal insufficiency[b,c]					
FIDELIO-DKD	ND	ND	ND	ND	ND
FIGARO-DKD	ND	ND	ND	ND	ND
Total	413	ND 2 (0.5)	374	ND 5 (1.3)	0.26 [0.05; 1.35]; 0.086
Sustained decrease in eGFR to < 15 ml/min/1.73m²				ND	
ESRD[d]				ND	
Decrease in eGFR by ≥ 57%				ND	
Renal death[e]				ND	
Cardiovascular morbidity (composite outcome) (supplementary information)					
FIDELIO-DKD	*ND*	*ND*	*ND*	*ND*	*ND*
FIGARO-DKD	*ND*	*ND*	*ND*	*ND*	*ND*
Total	*413*	*ND* *38 (9.2)*	*374*	*ND* *45 (12.0)*	*0.65 [0.42; 1.02];* *0.061*

Table 10: Results (mortality, morbidity, time to event) - RCT, direct comparison: finerenone + optimized standard therapy vs. placebo + optimized standard therapy, population with concomitant treatment with SGLT2 inhibitors or GLP-1 receptor agonists at baseline (multipage table)

Outcome category **outcome** **study**	**Finerenone + optimized standard therapy**		**Placebo + optimized standard therapy**		**Finerenone + optimized standard therapy vs. placebo + optimized standard therapy**
	N	**median time to event in months [95% CI]** **patients with event n (%)**	**N**	**median time to event in months [95% CI]** **patients with event n (%)**	**HR [95% CI]; p-value[a]**
Cardiovascular death				*ND*	
Non-fatal myocardial infarction				*ND*	
Non-fatal stroke				*ND*	
Severe heart failure events (operationalized as hospitalization for heart failure)				*ND*	

a. IPD meta-analysis: Cox regression model with factor "study" as fixed effect, stratified by region, UACR at the time of screening and cardiovascular history; as no information on the number of patients with events is available for the individual studies, these are presented for the meta-analysis.

b. The presentation of the individual components does not comprise the qualifying events, but all events that occurred during the course of the study.

c. Renal insufficiency was defined as the occurrence of ESRD or an eGFR < 15 ml/min/1.73m², confirmed by a 2nd measurement ≥ 4 weeks after the 1st measurement.

d. According to Module 4 B, ESRD was defined as:

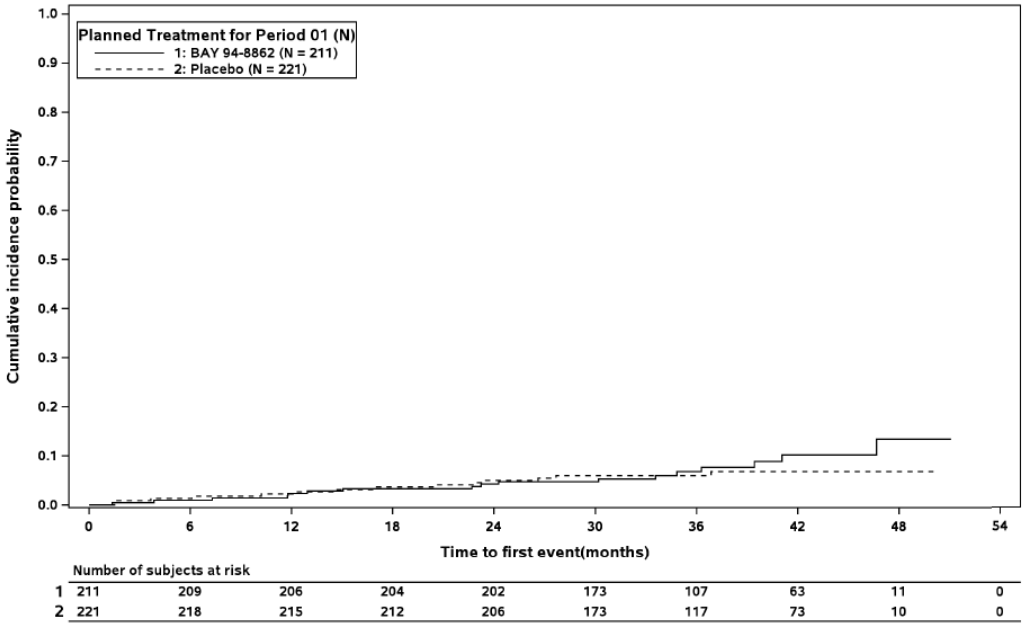
- Kidney transplant
- Peritoneal dialysis or haemodialysis required for at least 30 days and for which it is not apparent that treatment can be stopped after 90 days.
- Acute kidney injury resulting in dialysis or death and occurring during dialysis treatment.
- Renal replacement therapy indicated for symptomatic uraemia (eGFR of < 15 ml/min/1.73m^2 for at least 30 days) or asymptomatic uraemia (eGFR of < 8 ml/min/1.73m^2) but not available or accessible, refused or considered futile; ESRD is then diagnosed even without initiation of renal replacement therapy.

e. A death was classified as renal death if the patient died and had not received clinically indicated renal replacement therapy and there was no other probable cause of death.

CI: confidence interval; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; GLP-1: glucagon-like peptide 1; HR: hazard ratio; IPD: individual patient data; ND: no data; n: Number of patients with event; N: number of analysed patients; RCT: randomized controlled trial; SGLT2: sodium-glucose cotransporter 2; UACR: urine albumin-creatinine ratio

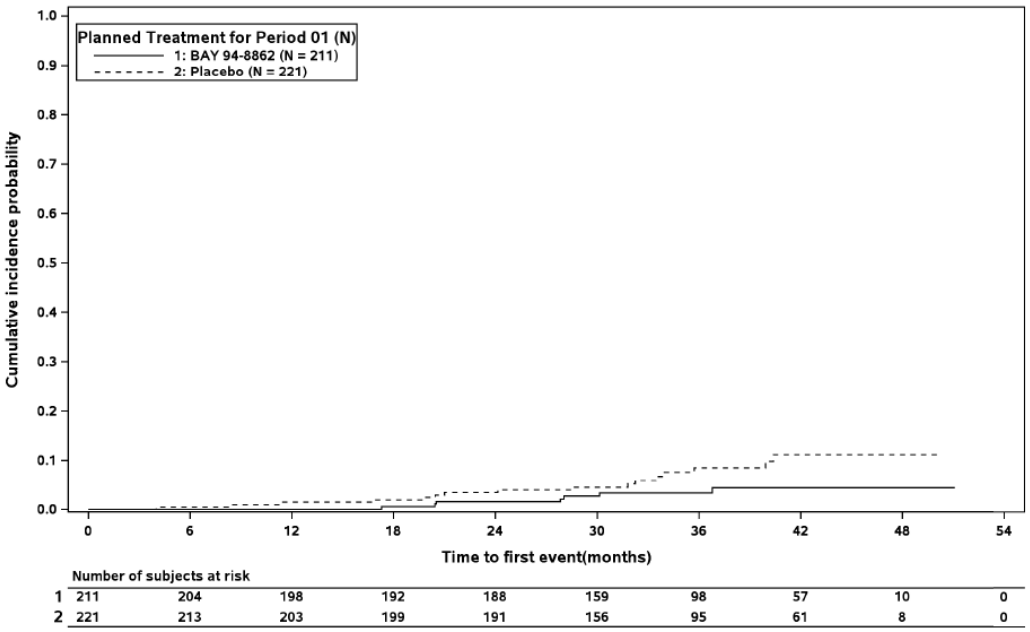
Appendix C Graphic display of the event time analyses presented (Kaplan-Meier curves)

C.1 Kaplan-Meier curves of the FIDELIO-DKD study



At-risk subject counts were calculated as at start of timepoint.

Figure 1: Kaplan-Meier curves for the outcome of all-cause mortality - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study



At-risk subject counts were calculated as at start of timepoint.

Figure 2: Kaplan-Meier curves for the supplementarily presented outcome of renal morbidity with eGFR decline ≥ 57% (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

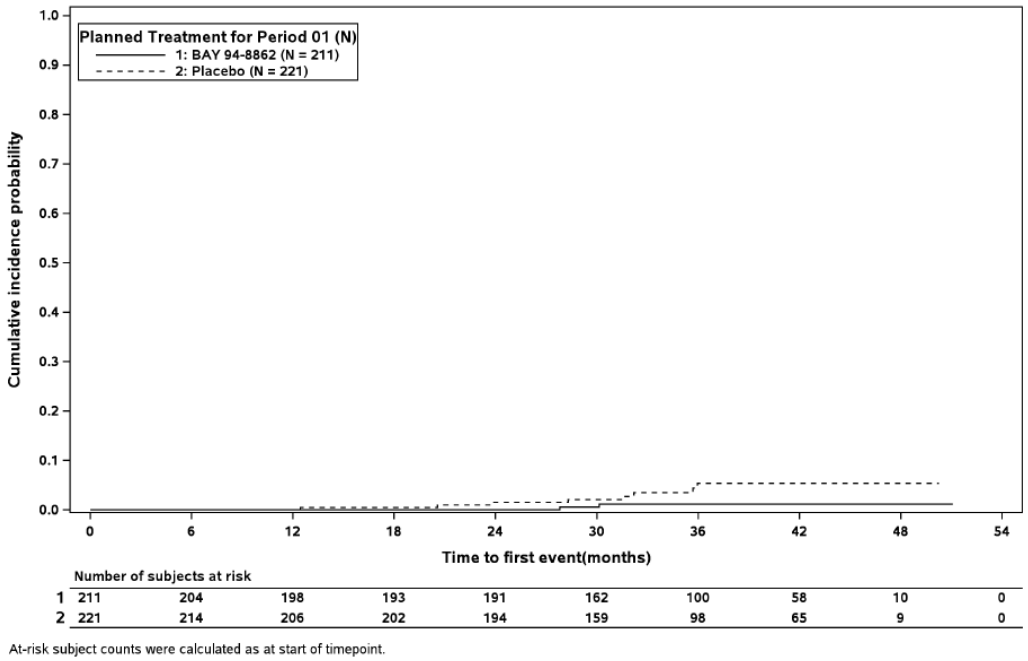


Figure 3: Kaplan-Meier curves for the individual component "renal insufficiency" (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

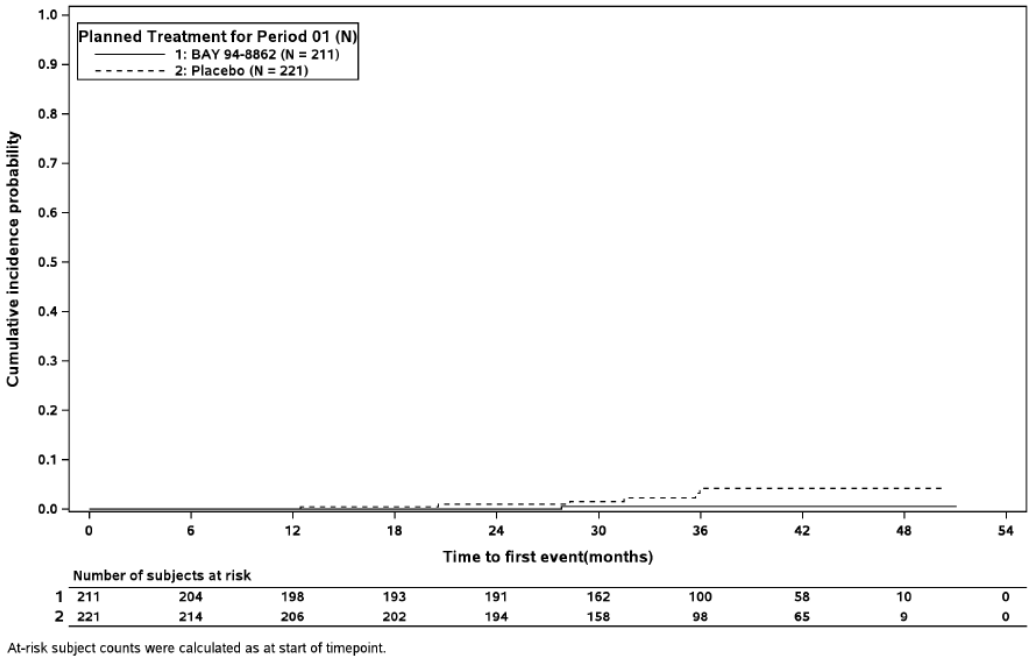


Figure 4: Kaplan-Meier curves for the individual component "sustained decrease in eGFR to < 15 ml/min/1.73m²" - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

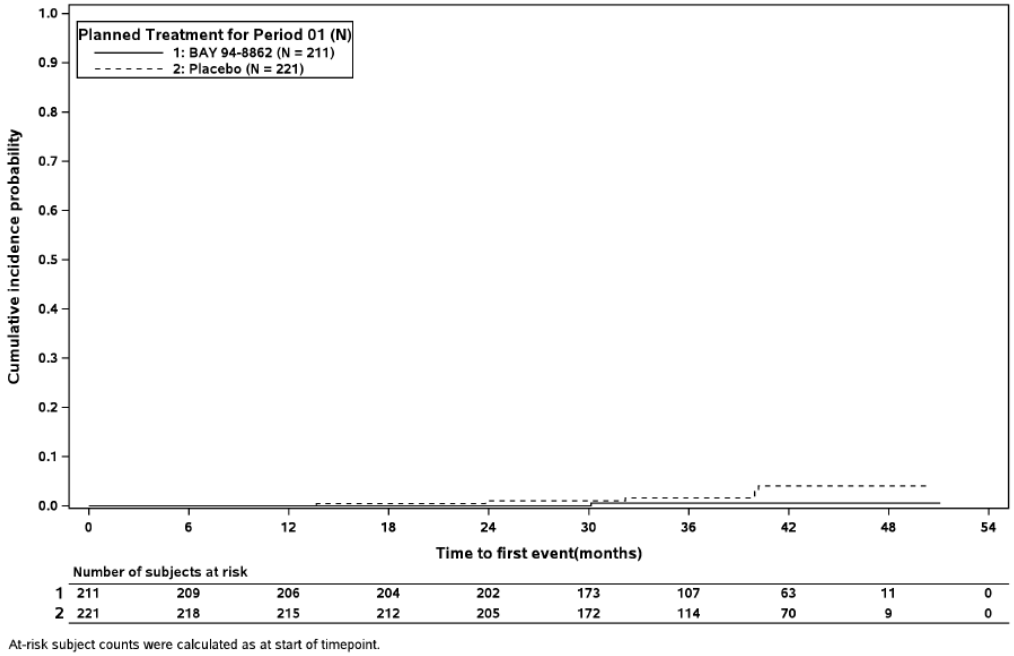


Figure 5: Kaplan-Meier curves for the individual component "ESRD – RCT", direct comparison: finerenone vs. placebo, FIDELIO-DKD study

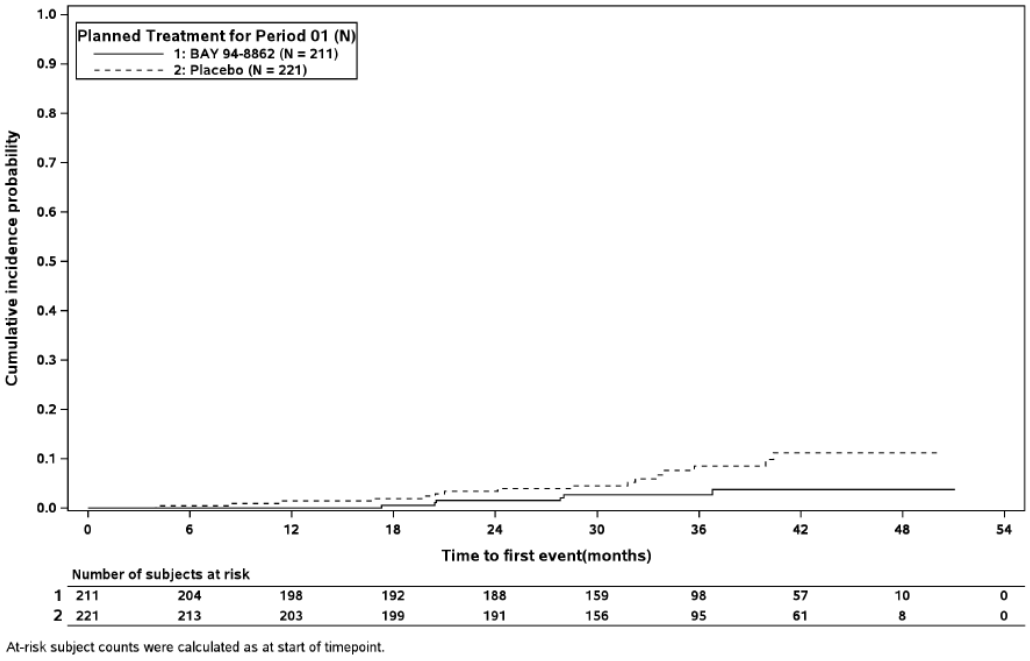


Figure 6: Kaplan-Meier curves for the supplementarily presented individual component "sustained decrease in eGFR by ≥ 57% from baseline - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

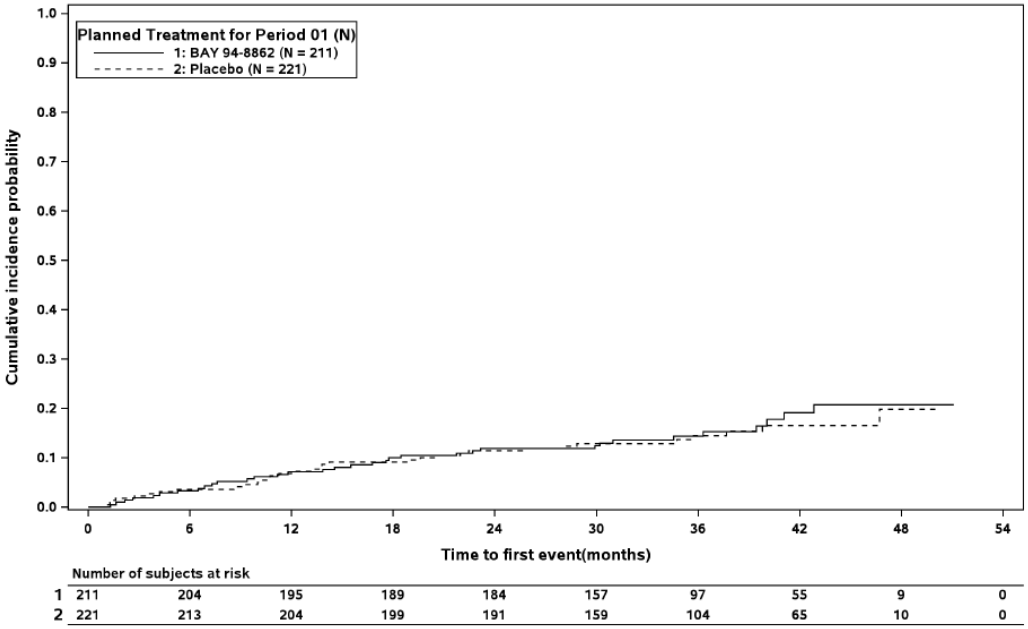


Figure 7: Kaplan-Meier curves for the supplementarily presented outcome of cardiovascular morbidity (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

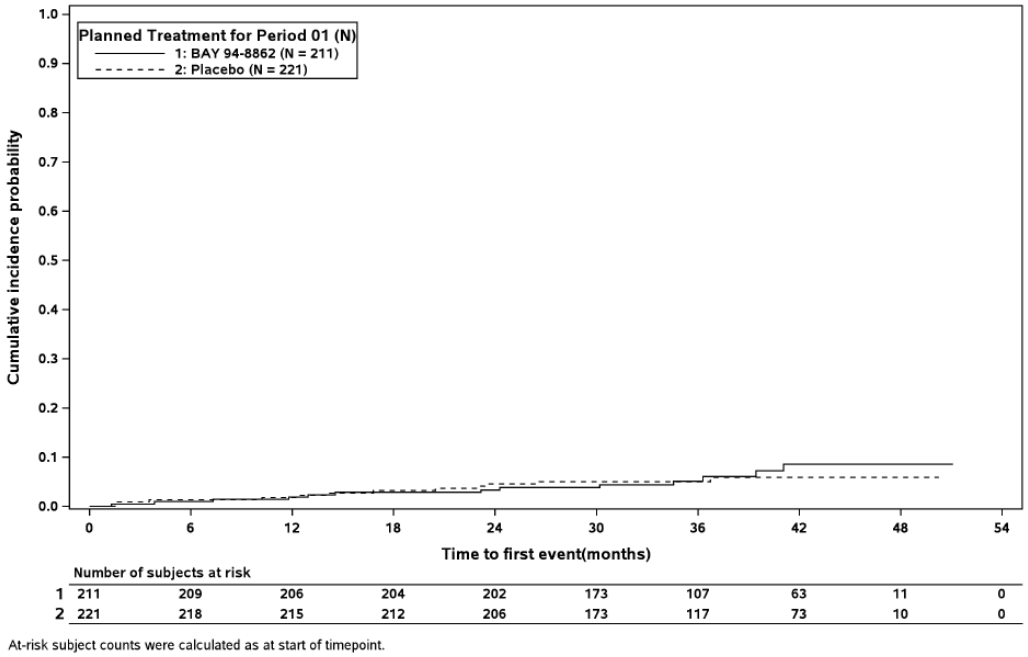


Figure 8: Kaplan-Meier curves for the supplementarily presented individual component “cardiovascular death” - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

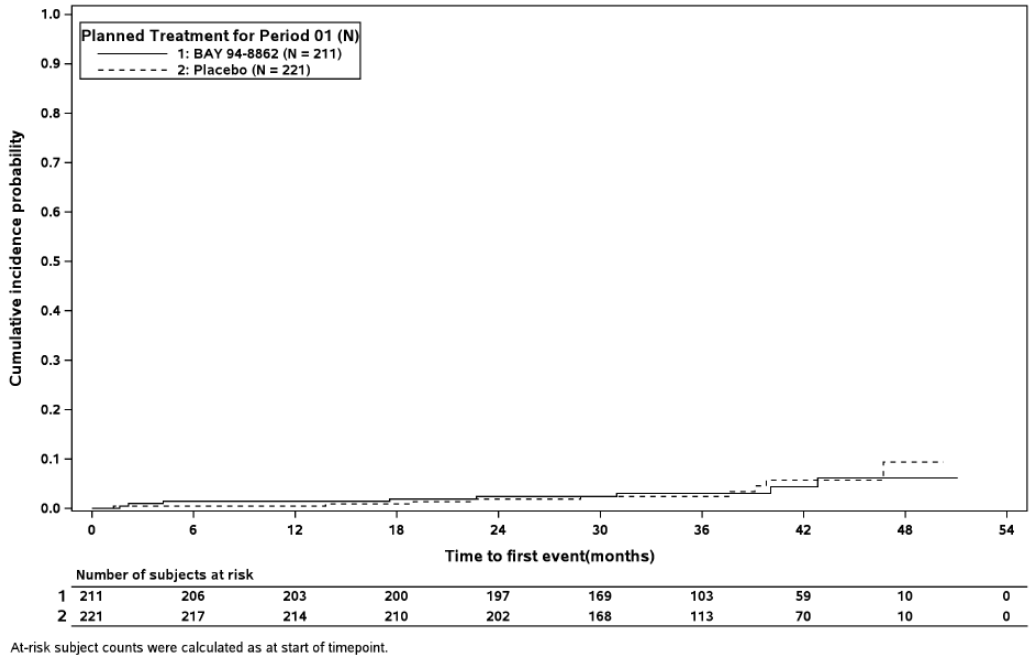


Figure 9: Kaplan-Meier curves for the supplementarily presented individual component "non-fatal myocardial infarction" - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

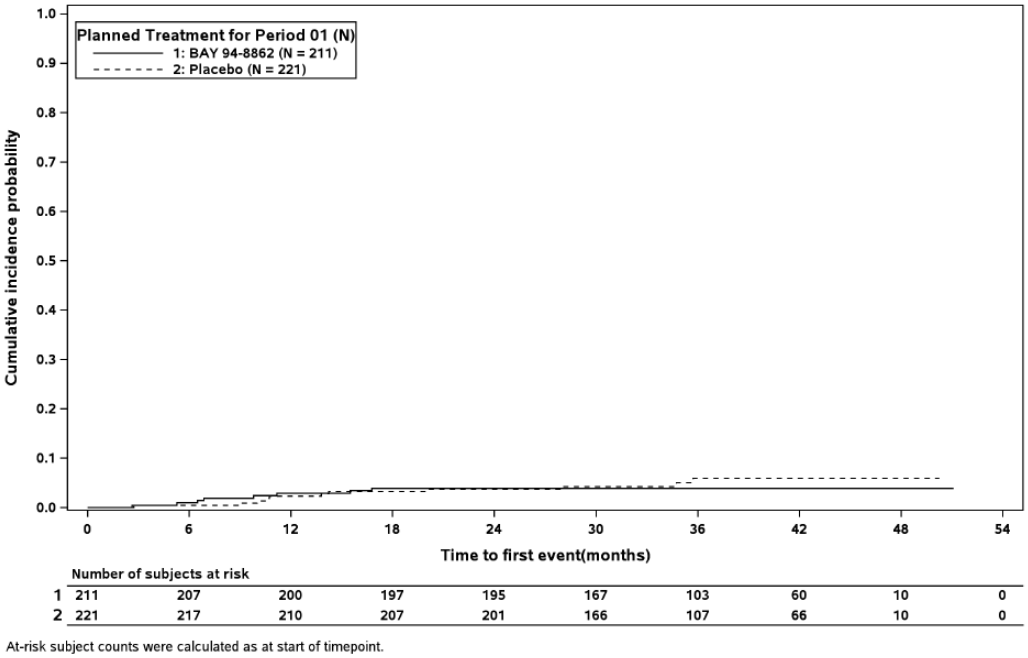


Figure 10: Kaplan-Meier curves for the supplementarily presented individual component "non-fatal stroke" - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

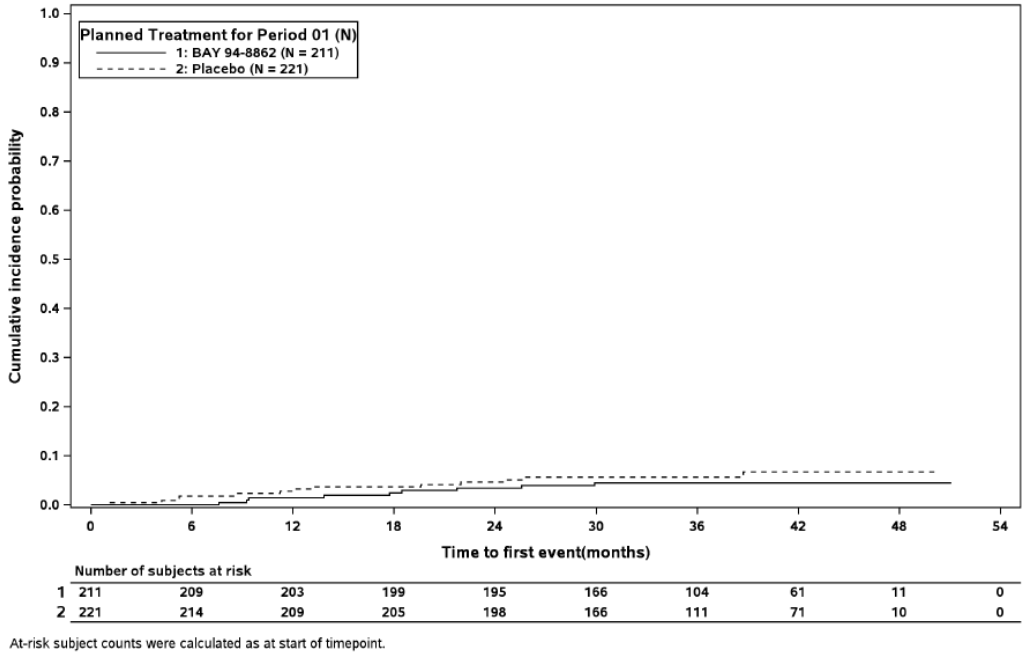


Figure 11: Kaplan-Meier curves for the supplementarily presented individual component "severe heart failure events" (operationalized as hospitalization for heart failure) - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

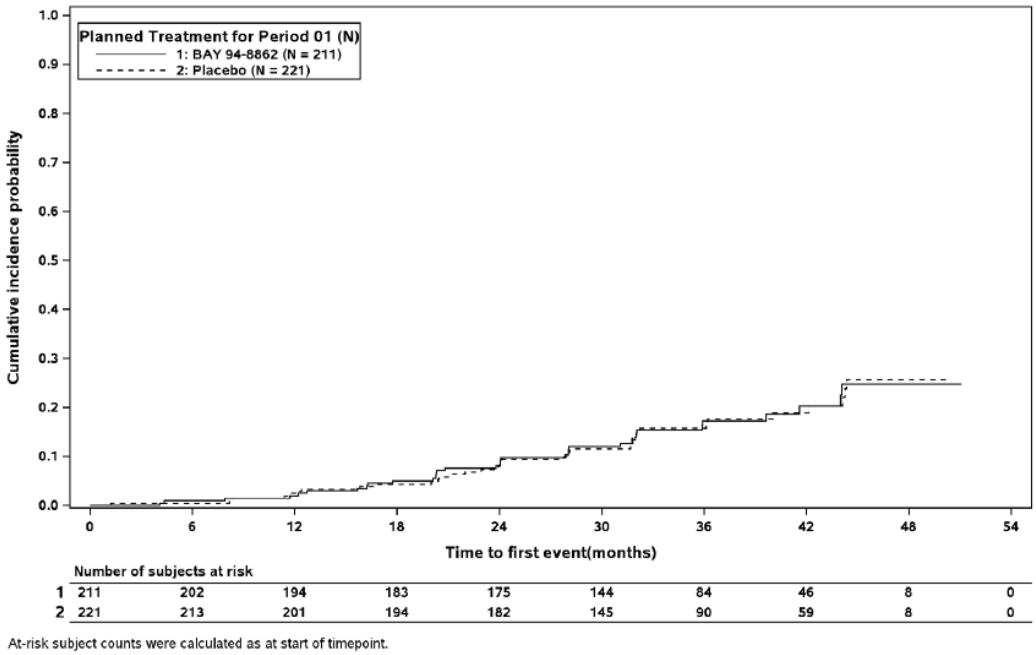


Figure 12: Kaplan-Meier curves for the supplementarily presented outcome of renal morbidity with decrease in eGFR ≥ 40% (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

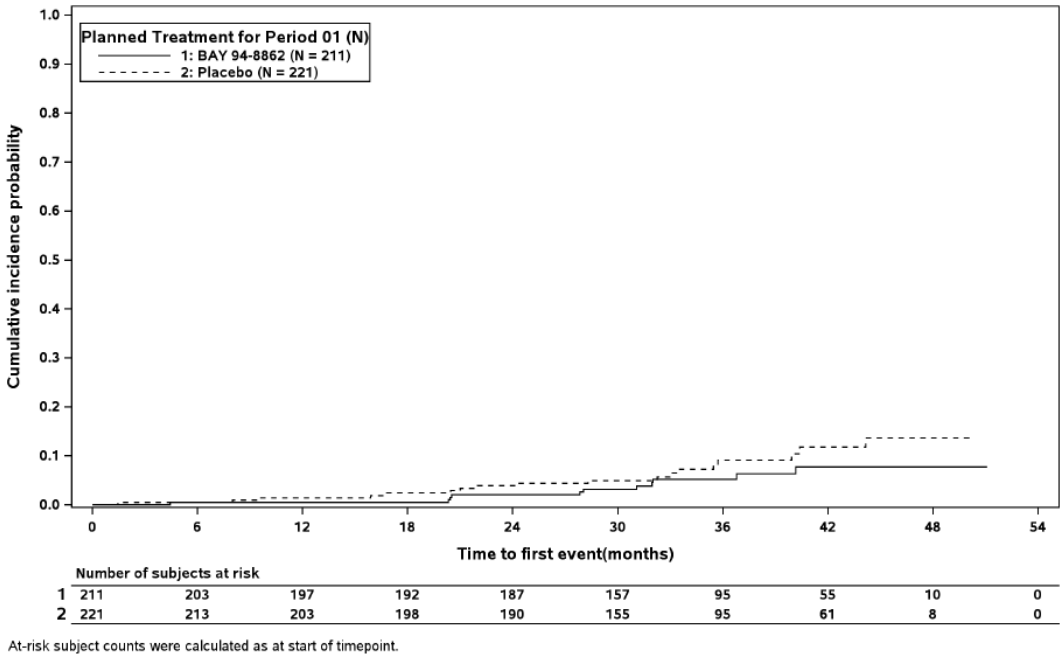


Figure 13: Kaplan-Meier curves for the supplementarily presented outcome of confirmed deterioration of CKD to stage 4 or 5 - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

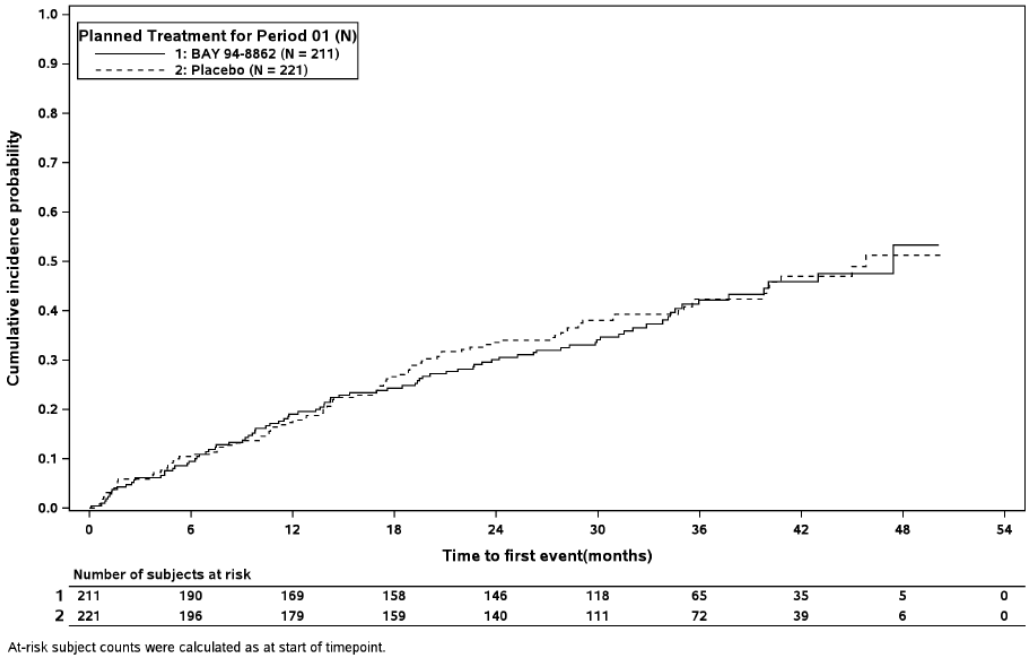
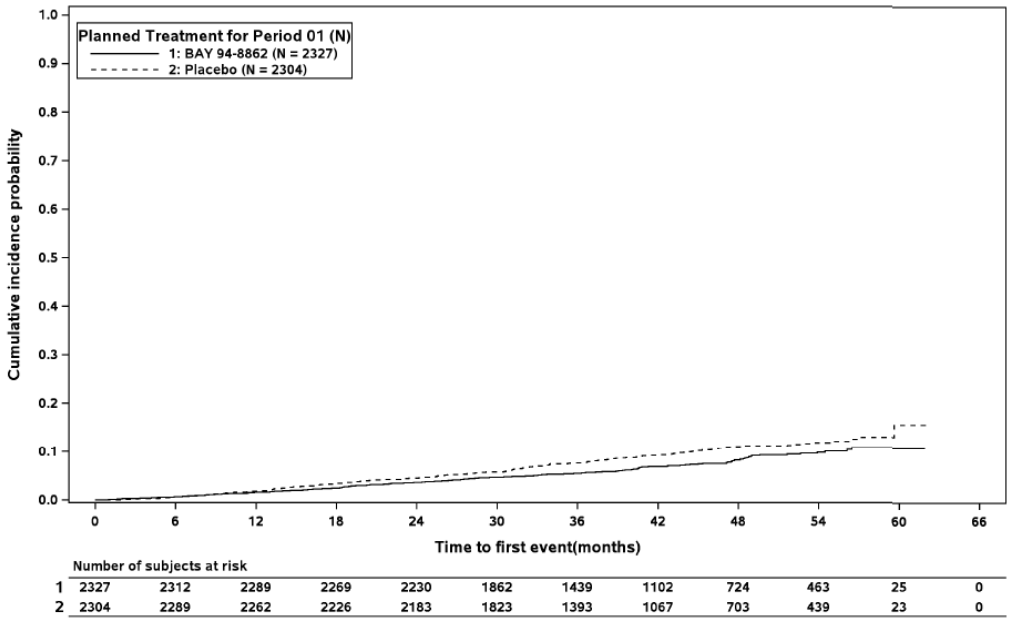


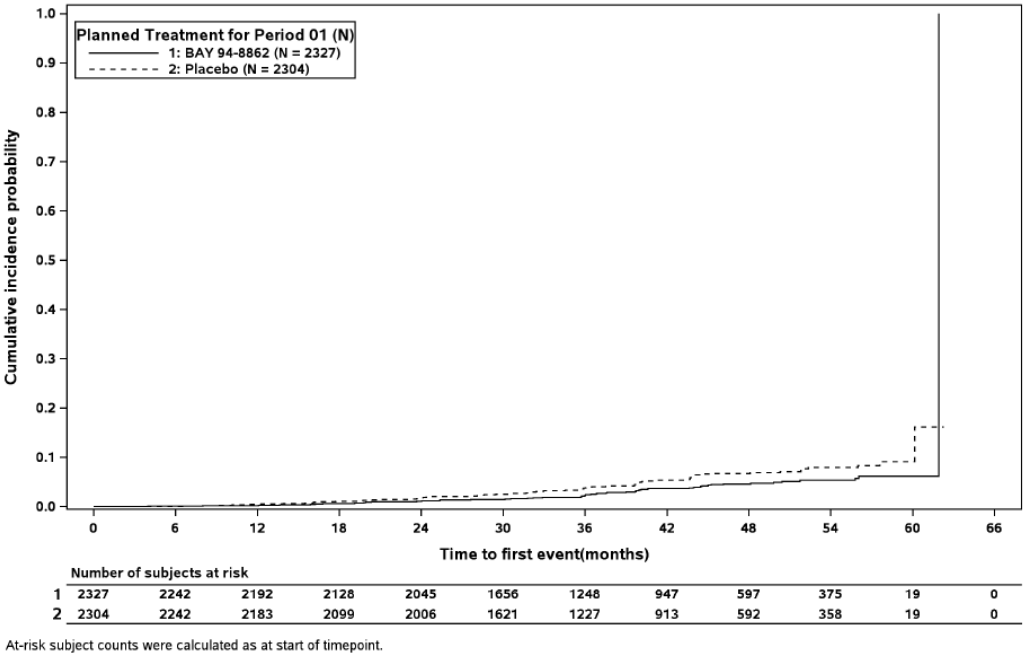
Figure 14: Kaplan-Meier curves for the supplementarily presented outcome of total hospitalization) – RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

C.2 Kaplan-Meier curves of the FIGARO-DKD study



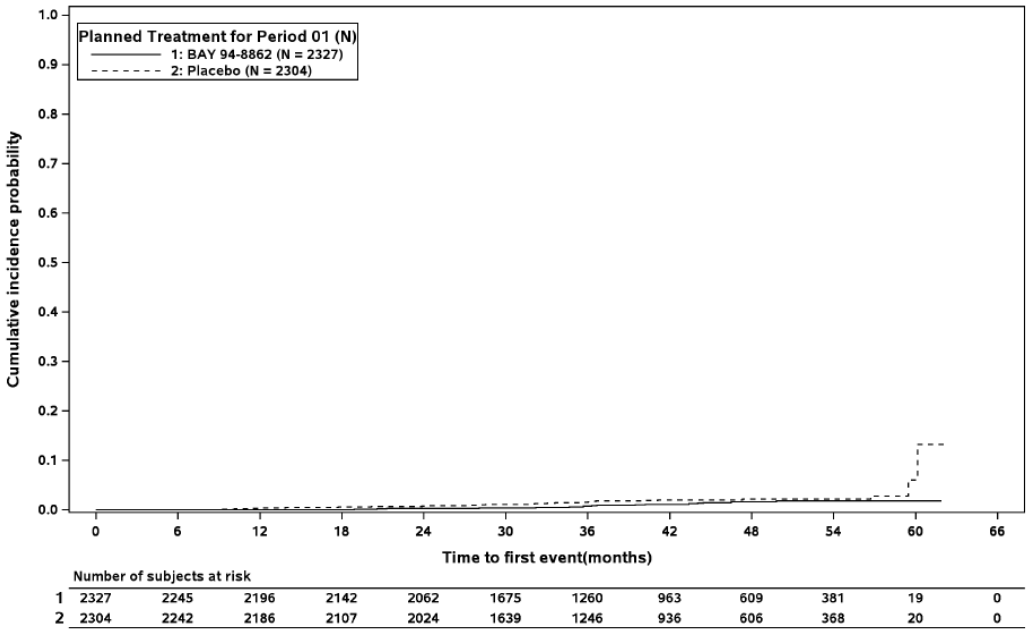
At-risk subject counts were calculated as at start of timepoint.

Figure 15: Kaplan-Meier curves for the outcome of all-cause mortality - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study



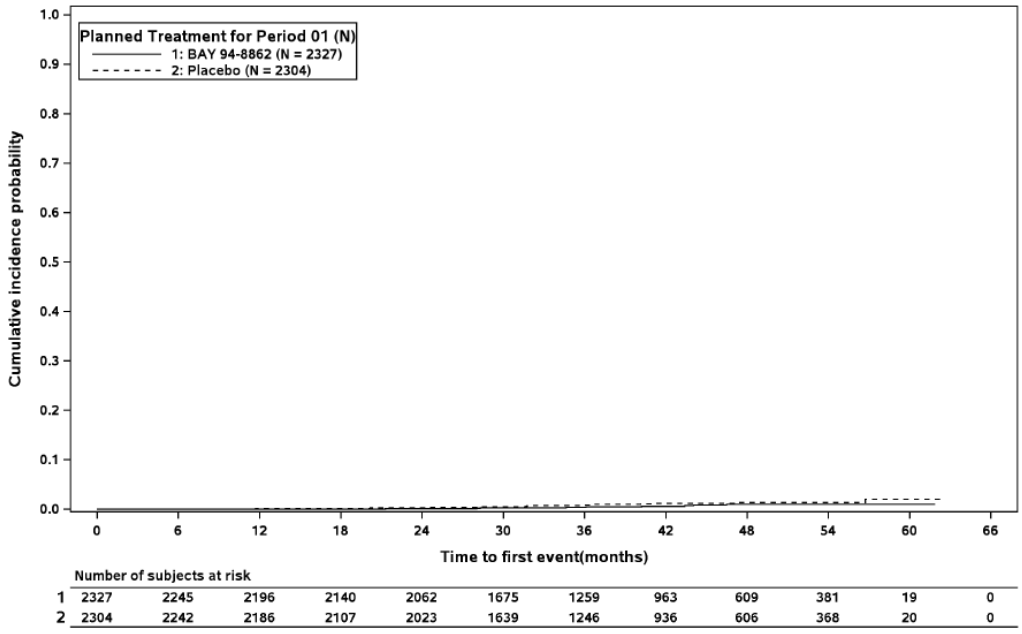
At-risk subject counts were calculated as at start of timepoint.

Figure 16: Kaplan-Meier curves for the supplementarily presented outcome of renal morbidity with decrease in eGFR ≥ 57% (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study



At-risk subject counts were calculated as at start of timepoint.

Figure 17: Kaplan-Meier curves for the individual component “renal insufficiency” (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study



At-risk subject counts were calculated as at start of timepoint.

Figure 18: Kaplan-Meier curves for the individual component “sustained decrease in eGFR to < 15 ml/min/1.73m²” - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study

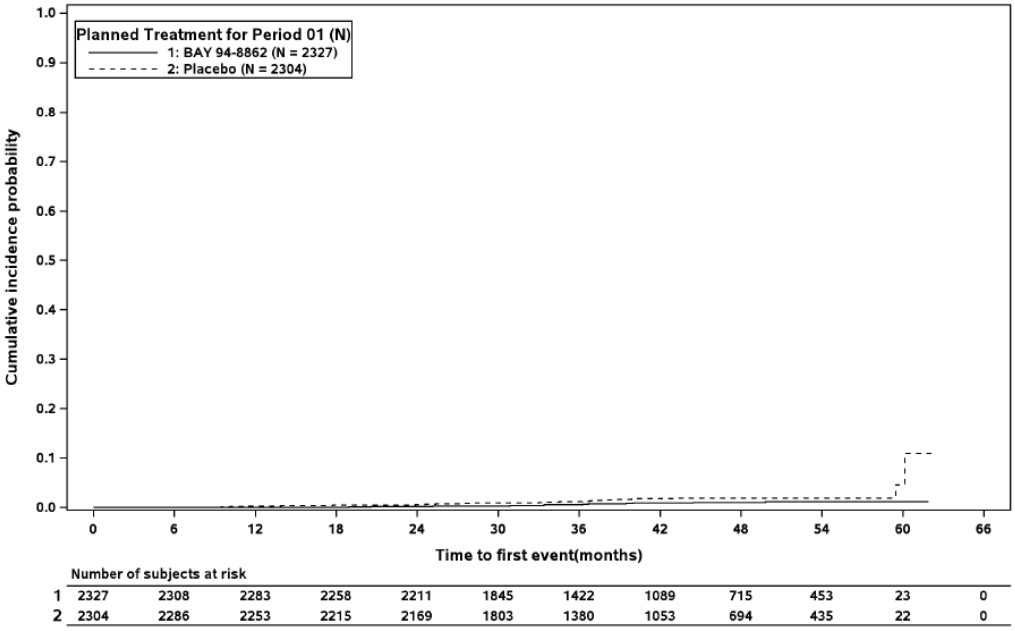


Figure 19: Kaplan-Meier curves for the individual component "ESRD" – RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study

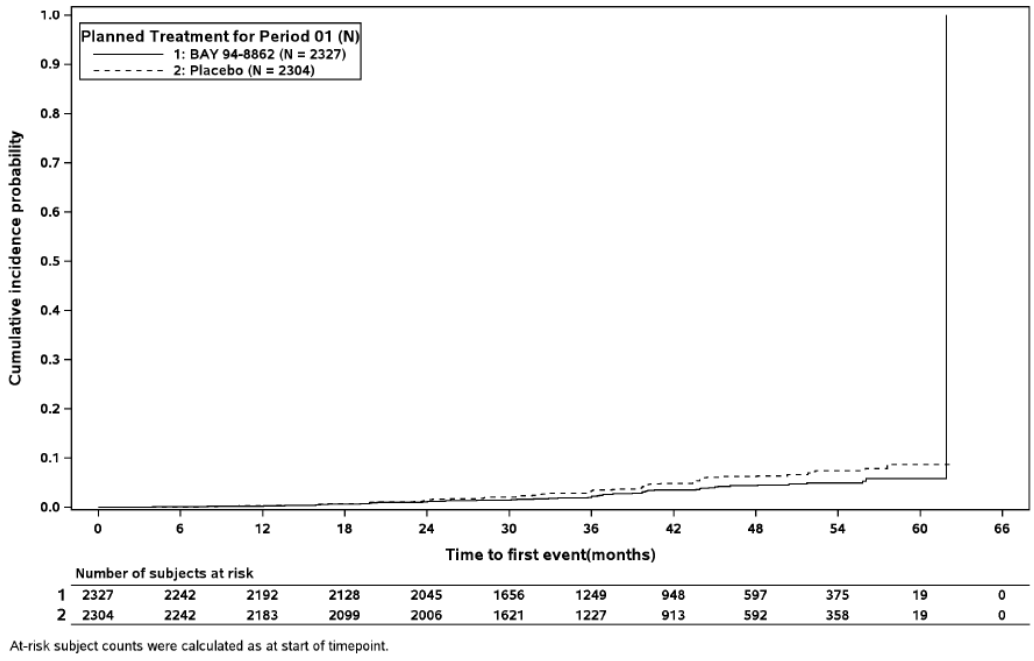


Figure 20: Kaplan-Meier curves for the supplementarily presented individual component "sustained decrease in eGFR by ≥ 57% from baseline - RCT, direct comparison: finerenone vs. placebo, FIDELIO-DKD study

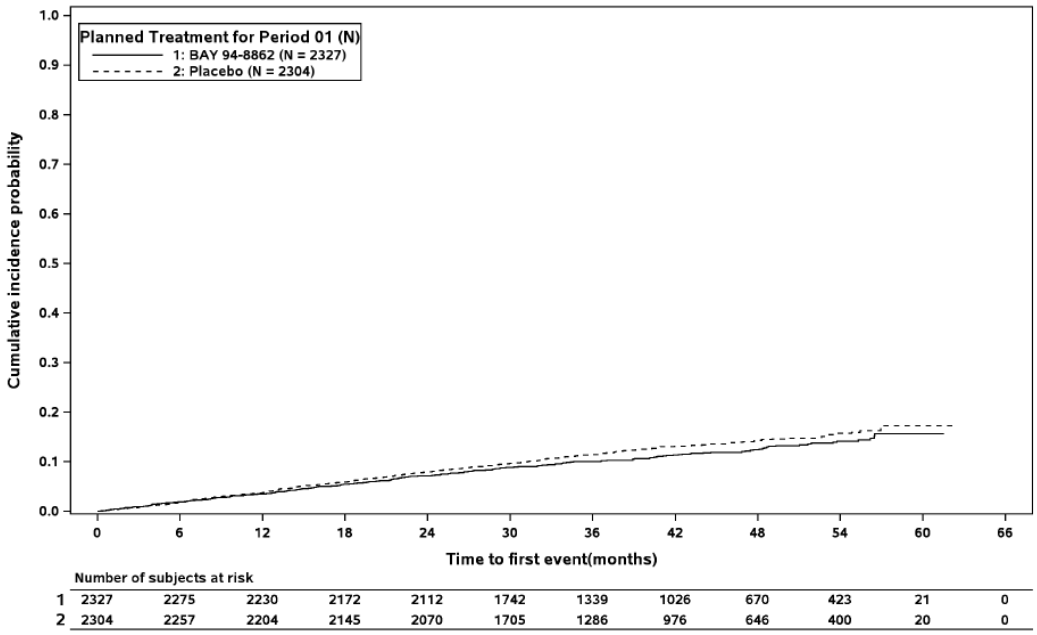


Figure 21: Kaplan-Meier curves for the supplementarily presented outcome of cardiovascular morbidity (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study

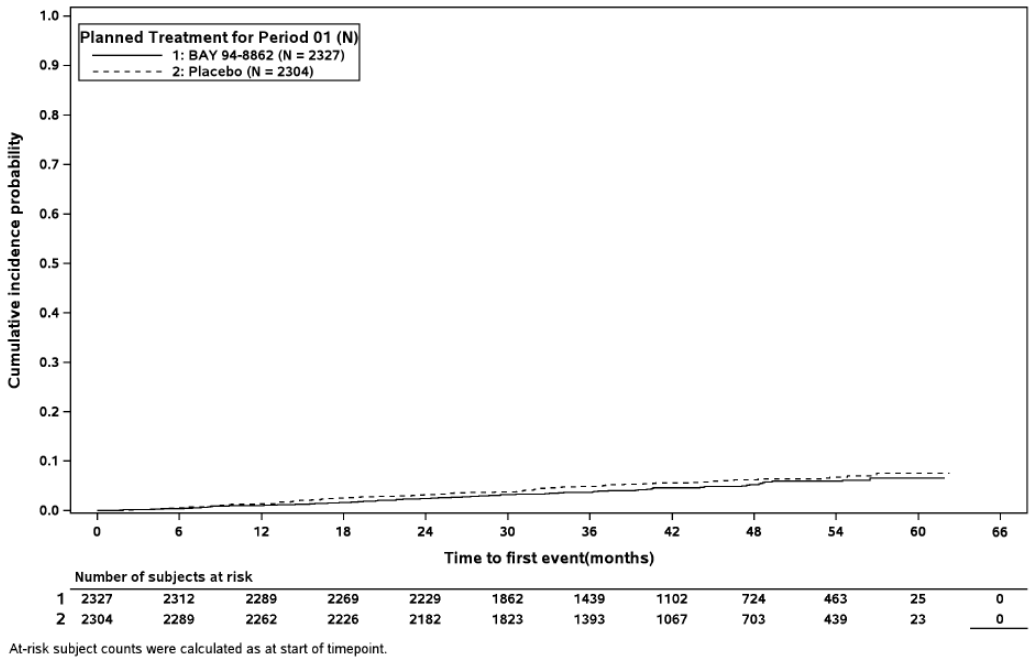


Figure 22: : Kaplan-Meier curves for the supplementarily presented individual component “cardiovascular death” - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study

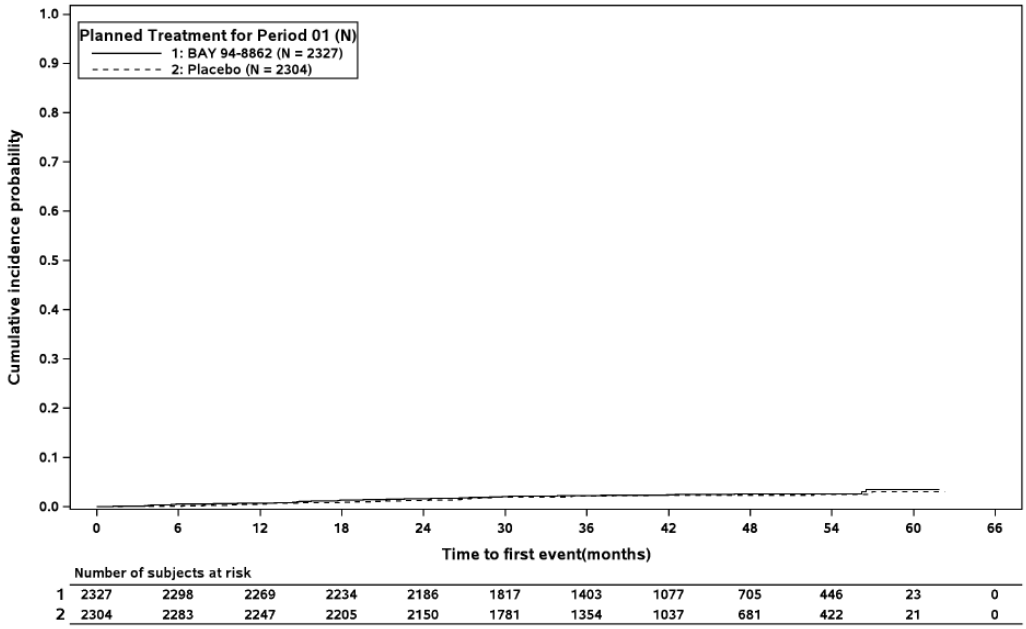


Figure 23: Kaplan-Meier curves for the supplementarily presented individual component "non-fatal myocardial infarction" - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study

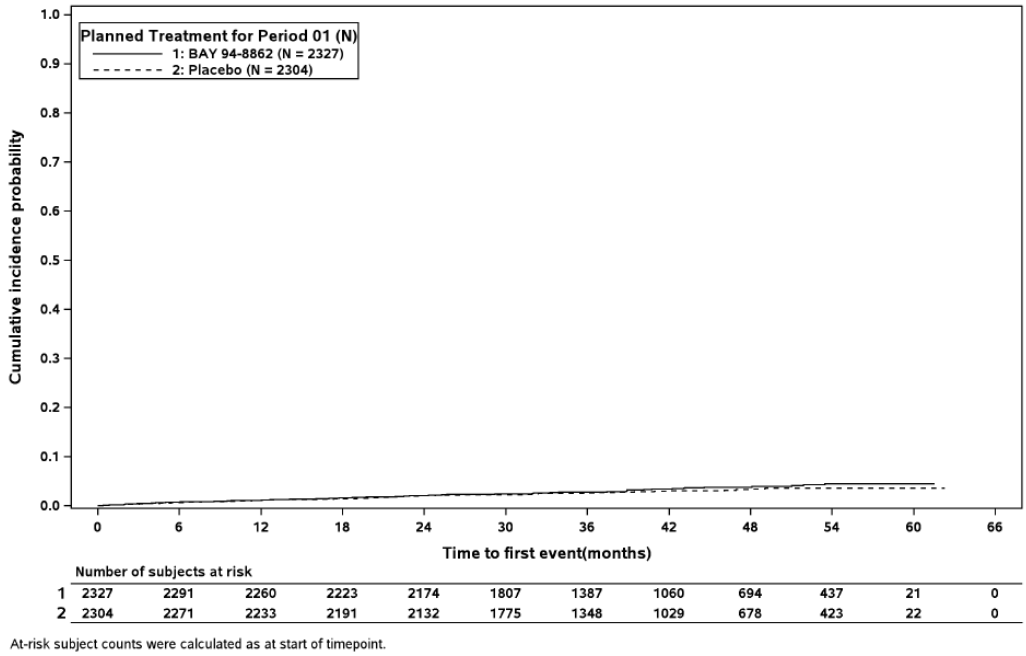
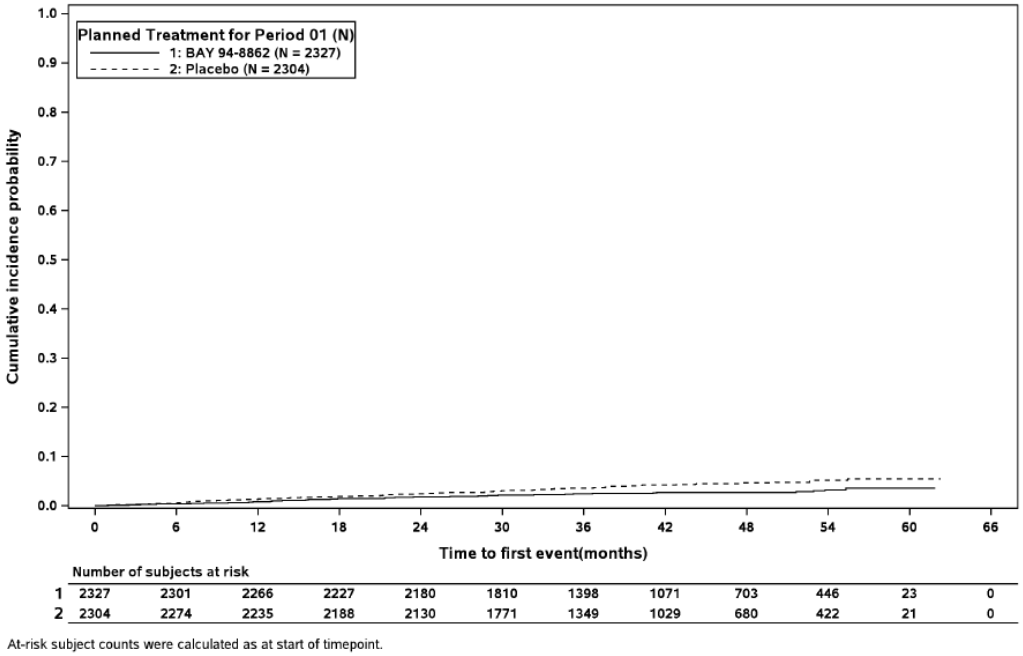
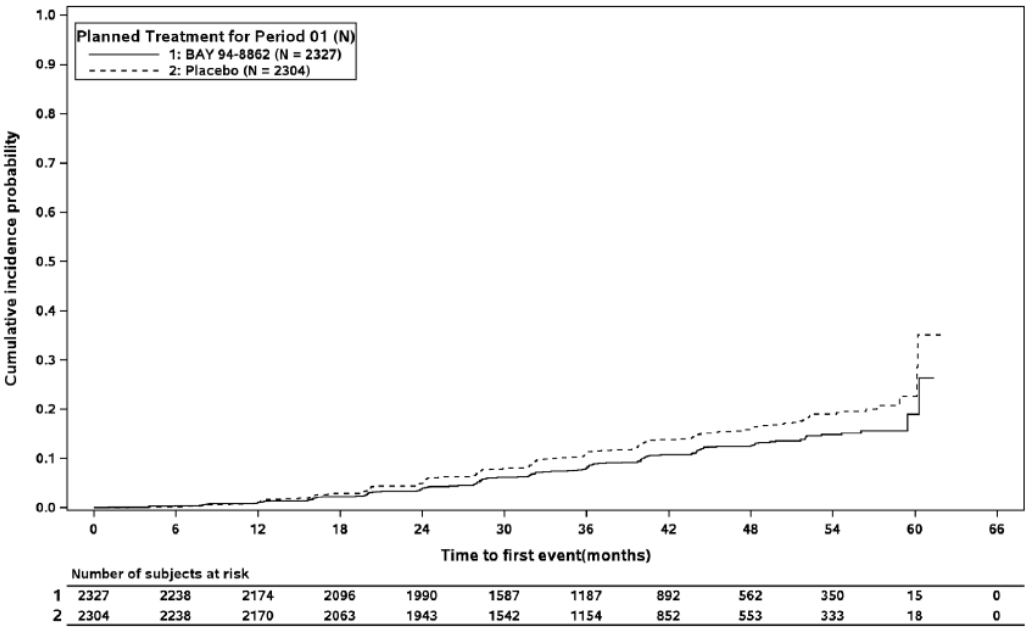


Figure 24: Kaplan-Meier curves for the supplementarily presented individual component "non-fatal stroke" - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study



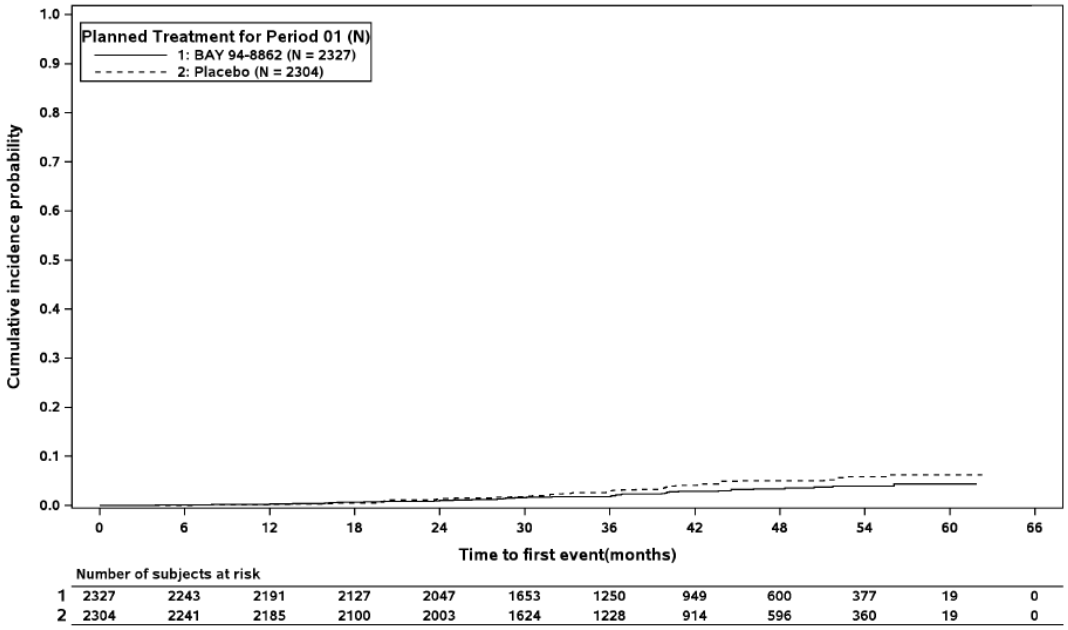
At-risk subject counts were calculated as at start of timepoint.

Figure 25: Kaplan-Meier curves for the supplementarily presented individual component "severe heart failure events" (operationalized as hospitalization for heart failure) - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study



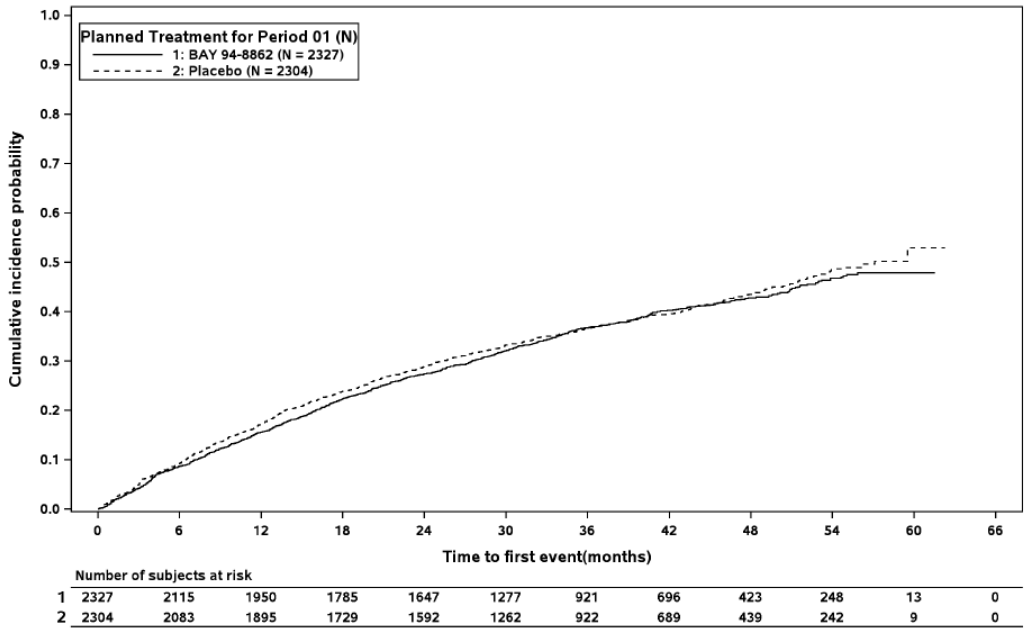
At-risk subject counts were calculated as at start of timepoint.

Figure 26: Kaplan-Meier curves for the supplementarily presented outcome of renal morbidity with decrease in eGFR ≥ 40% (composite outcome) - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study



At-risk subject counts were calculated as at start of timepoint.

Figure 27: Kaplan-Meier curves for the supplementarily presented outcome of confirmed deterioration of CKD to stage 4 or 5 - RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study



At-risk subject counts were calculated as at start of timepoint.

Figure 28: Kaplan-Meier curves for the supplementarily presented outcome of total hospitalization) – RCT, direct comparison: finerenone vs. placebo, FIGARO-DKD study