SYNOPSIS

Name of the Sponsor/Company: Krka, tovarna zdravil, d.d., Novo mesto.

Names of Finished Products:

Trade names of finished products vary depending on the country and strength of the product.

Perindopril/amlodipine/indapamide single-pill combination, tested in this study, appears in following trade names, in the countries where this study was conducted: Co-Amlessa, Co-Dalneva, Co-Dalnessa and Ко-Дальнева and Amlewel. Throughout this document, it is refered to as Co-Amlessa. Perindopril/amlodipine single-pill combination, tested in this study, appears in following trade names, in the countries where this study was conducted: Amlessa, Dalneva, Dalnessa and Дальнева. Throughout this document, it is refered to as Amlessa.

Names of Active Ingredients: perindopril (tert-butylamine perindoprilate), amlodipine (amlodipine besylate), indapamide

Title of Study: Fixed-Dose Combination of Perindopril/Amlodipine (Amlessa®) and Fixed-Dose Combination of Perindopril/Indapamide/Amlodipine (Co-Amlessa®) - Contribution to Management in newly diagnosed and uncontrolled hypertensive patients (PRECIOUS study)

Protocol no.: KCT 06/2017

Investigators and study centres:

Clinical study was conducted in seven countries: Armenia, Croatia, Hungary, Poland, Russian Federation, Serbia and Slovenia. Thirty-nine study sites have been initiated to participate in this study.

Studies period (years): 1.7 years **Date of first enrolment:** 12 February 2018 **Date of last completed:** 27 September 2019	**Phase of development:** Phase III/IV

Objectives:

The objectives of this trial were to evaluate the effect of therapy with Amlessa and Co-Amlessa on the blood pressure reduction and to evaluate the safety of the therapy in patients with essential AH who were antihypertensive treatment naïve and in patients with uncontrolled hypertension with previous mono, dual or triple antihypertensive treatment.

Methodology:

This study was an interventional, open-label, prospective, international, multi-centre, phase IIIb/IV clinical study. Study started with an initial screening visit (visit -1), to assess patient eligibility. One day later patients underwent study baseline visit (visit 1), during which baseline assessments were performed and/or completed. Eligible patients were assigned to treatment with one of the two study medication (Amlessa and Co-Amlessa arm), based on their previous antihypertensive therapy:

- antihypertensive medication naïve patients and patients on previous antihypertensive monotherapy were assigned to Amlessa arm,
- patients on previous dual antihypertensive therapy (including perindopril/amlodipine) and patients on previous triple antihypertensive therapy (other than perindopril/indapamid/amlodipine) were assigned to Co-Amlessa arm,
- patients on previous dual antihypertensive therapy (other than perindopril/amlodipine) were allocated to either Amlessa or Co-Amlessa arm at the investigators discretion, targeting the allocation ratio of 1:1.

Patients started taking the allocated study medication on day of the visit 1. The total active treatment duration was 16 weeks, divided into four treatment periods. The main four follow-up visits were performed at:

- visit 2/week 4 (following completion of first treatment period),
- visit 3/week 8 (following completion of second treatment period),

- visit 4/week 12 (following completion of third treatment period) and
- visit 5/week 16; final study visit (following completion of fourth treatment period).

At each of the three follow-up visits: week 4, week 8 and week 12, patient office blood pressure (BP) was measured and if normal office blood pressure (NBP) was achieved, the treatment with the study medication prescribed for the previous treatment period was continued. If NBP was not achieved at a particular follow-up visit (either visit 2, visit 3 or visit 4), study medication dosage was increased at that visit, in the following manner:

Amlessa Arm: Amlessa 4mg/5mg (initial therapy) → Amlessa 8mg/5mg → Amlessa 8mg/10mg → Co-Amlessa 8mg/10mg/2.5mg

Co-Amlessa Arm: Co-Amlessa 4mg/5mg/1.25mg (initial therapy) → Co-Amlessa 8mg/5mg/2.5mg → Co-Amlessa 8mg/10mg/2.5mg → end of study no further escalation of study medication dosage

NBP was defined as SBP < 140 mmHg and DBP < 90 mmHg; patients with type 2 diabetes mellitus: SBP < 140 mmHg and DBP < 85 mmHg. Assessments in this study included office BP and heart rate (HR) measurements, electrocardiogram (ECG), clinical laboratory tests (including hematology, lipids, biochemistry and liver function tests) as well as ambulatory blood pressure monitoring (ABPM). Completion of all the procedures at visit 5 determined the end of the patient's involvement in this clinical study.

Number of patients (planned and analysed):

It was planned that a total of 510 patients would conclude the efficacy assessments and a per-protocol population of 450 patients was planned. To allow for the estimated drop-out rate, up to 570 patients were expected to be screened.

Of the 572 subjects who were screened, 471 were assigned to study treatment. These 471 patients were analysed for main safety endpoints. A total of 450 patients provided sufficient efficacy data for inclusion to Full Analyses Set (FAS). A total of 277 patients were included in Per Protocol Set (PPS). FAS population was used as the main population for the assessment of study efficacy endpoints.

Diagnosis and main criteria for inclusion:

Men and women aged ≥ 18 years, able to adhere to study protocol, who have provided written informed consent were eligible for this study. Patients with essential arterial hypertension with entry office blood pressures as defined below were eligible:

- antihypertensive treatment naïve patients with entry SBP ≥150 mmHg AND/OR DBP ≥ 95 mmHg (SBP ≥ 150 AND/OR DBP ≥ 90 mmHg for patients with type 2 diabetes mellitus)
- uncontrolled patients on antihypertensive monotherapy, dual or triple antihypertensive therapy with entry SBP ≥140 mmHg AND/OR DBP ≥ 90 mmHg (SBP ≥ 140 AND/OR DBP ≥ 85 mmHg for patients with type 2 diabetes mellitus)

Test product product, dose and mode of administration, batch number:

- **Amlessa 4 mg/5 mg** tablets. Each tablet contains 4 mg perindopril tert-butylamine and 5 mg amlodipine (as amlodipine besilate). Oral use. *Batch numbers: D62511, D60766, D62335, D69274, D62389, D66122, D67749, D62334, 86351017.*
- **Amlessa 8 mg/5 mg** tablets. Each tablet contains 8 mg perindopril tert-butylamine and 5 mg amlodipine (as amlodipine besilate). Oral use. *Batch numbers: NE5751, NE3187, NE6003, NF5899, NE6043, NF1430, NF1435, NE6138, 86071017.*
- **Amlessa 8 mg/10 mg** tablets. Each tablet contains 8 mg perindopril tert-butylamine and 10 mg amlodipine (as amlodipine besilate). Oral use. *Batch numbers: NE5836, NE3648, NE6758, NF5079, NE3526, NF1479, NF3368, NE6659, 86041017.*
- **Co-Amlessa 4 mg/5 mg/1.25 mg** tablets. Each tablet contains 4 mg perindopril tert-butylamine, 5 mg amlodipine (as amlodipine besylate) and 1.25 mg indapamide. Oral use. *Batch numbers: NE6118, NE3414, NE6187, NF7475, NE6120, NE6119, NF7705, NE6055, 84720917.*

- **Co-Amlessa 8 mg/5 mg/2.5 mg** tablets. Each tablet contains 8 mg perindopril tert-butylamine, 5 mg amlodipine (as amlodipine besylate) and 2.5 mg indapamide. Oral use. *Batch numbers: NE7087, NE3593, NE6164, NF7754, NE6123, NE6168, NF1890, NE6021, 86891017.*

  Co-Amlessa 8 mg/10 mg/2.5 mg tablets. Each tablet contains 8 mg perindopril tert-butylamine, 10 mg amlodipine (as amlodipine besylate) and 2.5 mg indapamide. Oral use. *Batch numbers: NE5905, NE3101, NE5708, NF8009, NE5662, NE6833, NF2118, NE5704, 84580917*.

Duration of treatment:

The total active treatment duration was 16 weeks, with maximal allowed prolongation of three additional days per each active treatment period (in total up to 12 days) due to possible unpredicted causes for the delay in the follow-up visits.

Reference therapy, dose and mode of administration, batch number:

Not applicable. This study was open-label, non-comparative and un-controlled.

Criteria for evaluation:

Efficacy:

The following parameters were used to evaluate efficacy: office BP were performed at each study visit (representing primary and key secondary efficacy endpoint data; patient`s mean seated office measured SBP and DBP over the three consecutive BP measurements). ABPM was performed at baseline and visit 5 (representing secondary efficacy endpoint data, including: average 24h SBP and DBP, average awake-time SBP and DBP, average sleep-time SBP and DBP).

Safety:

The following parameters were used to evaluate safety: adverse events (AEs) were recorded and evaluated throughout the study and up to visit 5. Clinical laboratory tests were performed: hematology at visit 1 and 5, biochemistry and liver function tests at all study visits, except visit 4. Vital signs (HR, standing office BP) were performed at each study visits, while ECG was performed at screening only. Standard physical examinations were performed at screening and visit 5.

Statistical methods:

The efficacy analysis was performed on FAS and PPS, with the FAS as the primary analysis set. FAS was defined as the set of all screened patients who have received at least one dose of the study medication and have both baseline value and at least one post-baseline value of both SBP and DBP. PPS was defined as all subjects in the FAS who received any amount of study medication and have no important protocol deviations, have received the study-directed treatment, and have all assessments for all efficacy endpoints during the study.

The inferential part of statistical analysis was based on two-sided confidence intervals. Two-sided “equal-tails” Clopper-Pearson exact 95%-confidence intervals were calculated to estimate the population proportion of patients meeting a particular target BP endpoints. To evaluate endpoints related to mean absolute and relative baseline to visits differences in office BP and ABPM BPs, population mean absolute and relative differences were estimated using 95%-confidence interval based on the t-distribution or, in case of statistically significant departures from normality, the asymptotic 95%-confidence interval based on the normal (“z“) distribution.

When testing for equality of central tendencies, Shapiro-Wilk test was used to examine normality of data distribution. Shapiro-Wilk test showed non-normal data distribution, therefore Wilcoxon Signed Ranks Test was used to test for equality of central tendencies in PPS population, as sample sizes were equal for all variables at all visits. Summary statistics consisted of number of patients/observations, frequencies and corresponding percentages for categorical variables. The primary method of imputation of missing data was Last Observation Carried Forward (LOCF) approach.

Subject Disposition and Demography:

The number of patients treated, completed, discontinued from the study and analysed are summarized for each treatment arm in the table below.

	Amlessa Arm (no. patients)	Co-Amlessa Arm (no. patients)	All patients (no. patients)
Assigned to treatment (overall)	270	201	471
Assigned to treatment (FAS)	256	196	450
Completed (FAS)	234	185	419
Discontinued (FAS)	22	9	31
Reason: AE (FAS)	10	4	14
Other reasons (FAS)	12	5	17
Analyzed for efficacy			
FAS	256	194	450
PPS	161	116	277
Analyzed for AEs	270	201	471

In FAS, mean age was 54.0 ±12.4 years and mean BMI was 30.6 ±4.9 kg/m2. Notably more male (62.7%) than female (37.3%) patients were recruited to this study and included in FAS. At baseline, majority of patients in FAS had hypertension classified as grade 2 (44.7%) and grade 1 (44.2%). Baseline mean office seated SBP in FAS was 156.8 ±11.7 mmHg and baseline DBP was 98.0 ±8.7, with no major difference in mean baseline office seated SBP and DBP were in Amlessa and Co-Amlessa arm. In Amlessa arm, 51.2% of patients were antihypertensive treatment-naïve whereas in Co-Amlessa arm, patients have been switched to study medication from either previous dual (77.8%) or triple (22.2%) antihypertensive therapy.

Efficacy Results:

Office NBP (blood pressure target) was defined as office SBP < 140 mmHg and office DBP < 90 mmHg; patients with type 2 diabetes mellitus: office SBP < 140 mmHg and office DBP < 85 mmHg.

Primary efficacy endpoint

Proportion of patients reaching normal blood pressure (NBP) at visit 5 by Treatment Arm and Overall in FAS (LOCF imputation) [95% CI for population proportion, lower and upper CI]

Amlessa Arm (n=256)	*Co-Amlessa Arm (n=194)*	*FAS (n=450)*
77.7% [72.1%;82.7%]	83.0% [76.9%;88.0%]	80.0% [76.0%;83.6%]

Secondary efficacy endpoints:

1. Proportion of patients reaching NBP at visit 2, visit 3 and visit 4 by Treatment Arm and Overall in FAS (LOCF imputation) [95% CI for population proportion, lower and upper CI]

	Visit 2	*Visit 3*	*Visit 4*
Amlessa Arm (n=256)	48.8% [42.6%;55.1%]	64.1% [57.9%;69.9%]	74.6% [68.8%;79.8%]
Co-Amlessa Arm (n=194)	35.6% [28.8%;42.7%]	62.4% [55.1%;69.2%]	80.9% [74.7%;86.2%]
FAS (n=450)	43.1% [38.5%;47.8%]	63.3% [58.7%;67.8%]	77.3% [73.2%;81.1%]

2. Mean absolute (mmHg) and relative (%) change from baseline in office SBP and DBP after 4, 8, 12 and 16 weeks by Treatment and Overall in FAS (LOCF imputation) [95% CI for population means, lower and upper CI]

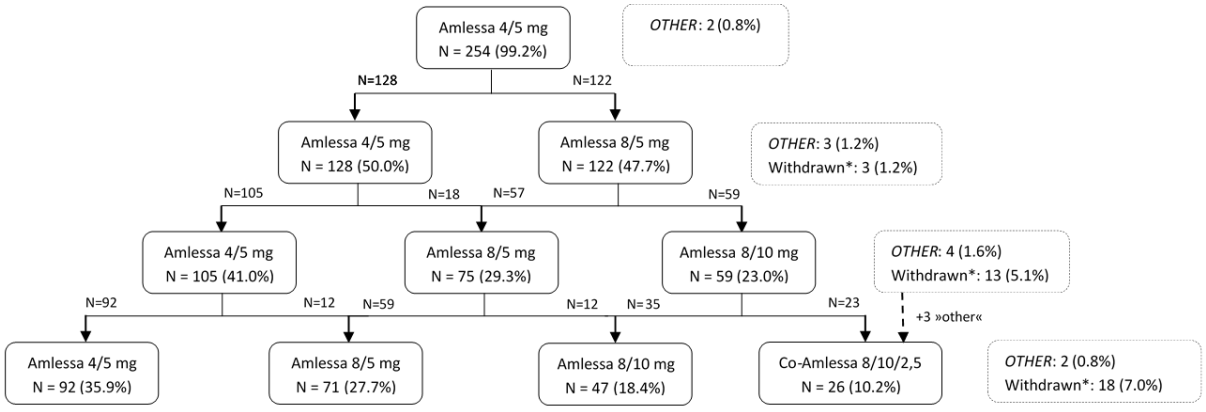
Amlessa Arm				
	Visit 2	**Visit 3**	**Visit 4**	**Visit 5**
SBP (mmHg)	n=256	n=256	n=256	n=256
	-17.1 [-18.8;-15.3]	-21.1 [-22.8;-19.4]	-23.6 [-25.2;-22]	-26.8 [-28.4;-25.2]
	-10.6% [-11.7%;-9.6%]	-13.3% [-14.3%;-12.2%]	-14.8% [-15.8%;-13.9%]	-16.9% [-17.8%;-16%]
DBP (mmHg)	n=256	n=256	n=256	n=256
	-10.9 [-12.1;-9.7]	-13.3 [-14.4;-12.2]	-15.1 [-16.2;-13.9]	-16.6 [-17.6;-15.5]
	-10.7% [-11.9%;-9.6%]	-13.1% [-14.2%;-12.1%]	-15.0% [-16%;-13.9%]	-16.5% [-17.5%;-15.6%]
Co-Amlessa Arm				
	Visit 2	**Visit 3**	**Visit 4**	**Visit 5**
SBP (mmHg)	n=194	n=194	n=194	n=194
	-14.4 [-16.5;-12.2]	-20.9 [-23.2;-18.7]	-25.5 [-27.6;-23.5]	-28.8 [-31;-26.5]
	-8.7% [-10%;-7.5%]	-12.9% [-14.3%;-11.6%]	-15.8% [-17%;-14.6%]	-17.9% [-19.2%;-16.6%]
DBP (mmHg)	n=194	n=194	n=194	n=194
	-9.0 [-10.5;-7.5]	-13.2 [-14.7;-11.7]	-15.0 [-16.4;-13.6]	-16.7 [-18.2;-15.2]
	-8.7% [-10.2%;-7.2%]	-13% [-14.5%;-11.6%]	-14.8% [-16.1%;-13.6%]	-16.6% [-18%;-15.2%]
Complete FAS				
	Visit 2	**Visit 3**	**Visit 4**	**Visit 5**
SBP (mmHg)	n=450	n=450	n=450	n=450
	-15.9 [-17.2;-14.5]	-21 [-22.4;-19.7]	-24.4 [-25.7;-23.2]	-27.7 [-29;-26.3]
	-9.8% [-10.6%;-9%]	-13.1% [-13.9%;-12.3%]	-15.2% [-16%;-14.5%]	-17.3% [-18.1%;-16.5%]
DBP (mmHg)	n=450	n=450	n=450	n=450
	-10.1 [-11;-9.1]	-13.2 [-14.2;-12.3]	-15.0 [-15.9;-14.2]	-16.6 [-17.5;-15.7]
	-9.9% [-10.8%;-8.9%]	-13.1% [-14%;-12.2%]	-14.9% [-15.7%;-14.1%]	-16.6% [-17.4%;-15.7%]

3. Mean absolute (mmHg) and relative (%) changes from baseline to 16 weeks in average 24-hour SBP and DBP, average awake time SBP and DBP, and average sleep time SBP and DBP (LOCF imputation) [95% CI for population means, lower and upper CI]

	Amlessa Arm	*Co-Amlessa Arm*	*FAS*
24h average SBP (mmHg)	n=256	n=194	n=450
	-16.1 [-17.6;-14.6]	-21.8 [-23.8;-19.9]	-18.6 [-19.8;-17.4]
	-11.1% [-12%;-10.1%]	-14.5% [-15.7%;-13.3%]	-12.5% [-13.3%;-11.8%]
24h average DBP (mmHg)	n=256	n=194	n=450
	-10.8 [-11.9;-9.7]	-13.5 [-14.8;-12.3]	-12.0 [-12.8;-11.2]
	-11.3% [-12.4%;-10.2%]	-14.2% [-15.5%;-13%]	-12.5% [-13.4%;-11.7%]
Awake-time average SBP (mmHg)	n=256	n=194	n=450
	-16.6 [-18.2;-15]	-22.9 [-25;-20.8]	-19.3 [-20.6;-18]
	-11.1% [-12.1%;-10.1%]	-14.9% [-16.1%;-13.6%]	-12.7% [-13.5%;-11.9%]
Awake-time average DBP (mmHg)	n=256	n=194	n=450
	-10.8 [-12;-9.7]	-14.2 [-15.5;-12.9]	-12.3 [-13.2;-11.4]
	-10.9% [-12.1%;-9.8%]	-14.4% [-15.7%;-13.1%]	-12.4% [-13.3%;-11.6%]
Sleep-time average SBP (mmHg)	n=256	n=194	n=450
	-14.6 [-16.3;-12.8]	-18.7 [-20.9;-16.6]	-16.4 [-17.7;-15]
	-10.4% [-11.6%;-9.2%]	-13.1% [-14.5%;-11.6%]	-11.6% [-12.5%;-10.6%]
Sleep-time average DBP (mmHg)	n=256	n=194	n=450
	-10.3 [-11.5;-9]	-11.5 [-13;-10.1]	-10.8 [-11.8;-9.9]
	-11.4% [-12.8%;-10.1%]	-12.9% [-14.5%;-11.2%]	-12.1% [-13.1%;-11%]

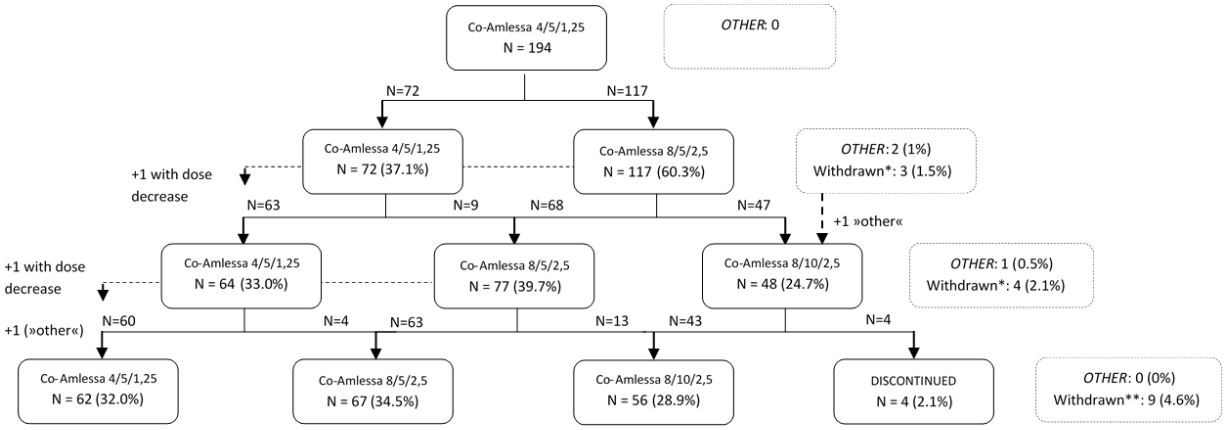
Treatment Pathways

In FAS analysis set 254 patients received Amlessa 4/5 mg at visit 1. Two patients have been misallocated to treatment at Visit 1 (one received Amlessa 8/5 mg, the other received Amlessa 8/10 mg). In Amlessa arm the two major up-titrations steps were at Visit 2 and (to a lesser extent) Visit 3, whereas at last possible up-titration step in this study (Visit 4) 186 of 256 (72.6%) Amlessa arm patients have maintained their previously dispensed medication dosage.



** total cummulative number of patients withdrawn at or up to visits 1-4 (and not dispensed IMP)*

In FAS analysis set 194 patients received Co-Amlessa 4/5/1.25 mg at visit 1. In Co-Amlessa arm the two major up-titrations steps were at Visit 2 and (to a lesser extent) Visit 3, whereas at last possible up-titration step in this study (Visit 4) 166 of 194 (86.9%) Co-Amlessa arm patients have maintained their previously dispensed medication dosage.



** total cummulative number of patients withdrawn at or up to visits 1-3 (and not dispensed IMP)*

*** total cummulative number of patients withdrawn at or up to visit 4 including 4 patients who were discontined due to non-achievement of BP goal at visit 4*

Safety Results:

Out of 471 patients in SAS, 14.6% of patients reported AE. Proportion of patients with any reported AE in Amlessa arm was 16.7% and proportion in Co-Amlessa arm was 11.9%. Proportion of patients with any report of ADR was lower: 10.4% in complete SAS, 12.2% in Amlessa arm and 8.0% in Co-Amlessa arm.

The most prevalent treatment emergent non-serious AE in Amlessa arm (n=270) were Cough (3.0% total related, 0.4% total unrelated), Oedema peripheral (1.5% total related), Blood potassium increased (1.9% total related) and Gamma-glutamyltransferase increased (1.1% total related, 0.4% total unrelated). The most prevalent treatment emergent non-serious AE in Co-Amlessa arm (n=201) were Cough (1.5% total related), Hypotension (1.5% total related), Gamma-glutamyltransferase increased (1.0% total related, 1.5% total unrelated), Alanine aminotransferase increased (1,0% total related, 1.5% total unrelated) and Blood potassium decreased (1.0% total related).

There were no reports of deaths in this study. Two patients with treatment emergent SAE were recorded: breast cancer in one Co-Amlessa arm patient and back pain (leading to surgical intervention) in one Amlessa arm patient. Both events were assessed as not related to treatment by the investigators. A total of 12 (4.4%) patients in Amlessa arm have withdrawn or have been discontinued from the study due to AE or due to the need for major surgical intervention. The most prevalent TEAEs leading to study discontinuation in Amlessa arm (n=270) were Cough (four patients) and Oedema peripheral (two patients), while all other related events were recorded for a single patient. These included: Urtikaria, Sciatica, Nervousness, Vomiting and Headache [1 patient], Rash and Lip oedema [1 patient], back pain [serious not-related AE], for one patient Abdomina pain in addition to Cough was reported as reason for discontinuation. Four AEs leading to study discontinuation were recorded in Co-Amlessa arm (n=201): Rash erythematous, Urticaria, Blood potassium increased and Breast cancer (serious not-related AE). Each of these events was recorded in a single patient.

The mean absolute changes in safety laboratory assessments (ALT, AST, GGT, creatinine, potassium, eGFR as well as hematological laboratory parameters) from baseline to follow-up visits, observed in this study, were small. The mean absolute changes between seated and standing office SBP and DBP, measured at each study visit, were small.

1. Summaries of Safety Laboratory Assessment Measurements at visits 1, 2, 3 and 5 for in Amlessa Arm and Co-Amlessa Arm in SAS

		Amlessa Arm		Co-Amlessa Arm	
		n	**Mean (SD)**	***n***	**Mean (SD)**
ALT (µkat/L)	Visit 1	267	0.6 (0.3)	200	0.5 (0.3)
	Visit 2	254	0.5 (0.3)	193	0.5 (0.3)
	Visit 3	249	0.5 (0.6)	192	0.5 (0.5)
	Visit 5	234	0.5 (0.3)	187	0.5 (0.3)
AST (µkat/L)	Visit 1	267	0.5 (0.2)	200	0.4 (0.2)
	Visit 2	254	0.4 (0.2)	193	0.4 (0.2)
	Visit 3	246	0.4 (0.1)	192	0.4 (0.3)
	Visit 5	234	0.4 (0.2)	187	0.4 (0.2)
GGT (µkat/L)	Visit 1	266	0.7 (0.5)	199	0.7 (0.5)
	Visit 2	254	0.7 (0.5)	192	0.7 (0.8)
	Visit 3	248	0.7 (0.8)	191	0.7 (1.0)
	Visit 5	234	0.6 (0.5)	187	0.7 (0.9)
Creatinine (µmol/L)	Visit 1	267	76.8 (15.2)	200	76.2 (14.9)
	Visit 2	254	76.2 (15.1)	193	78.1 (15.0)
	Visit 3	249	76.4 (13.7)	191	78.9 (14.6)
	Visit 5	234	77.5 (14.2)	187	79.1 (15.7)
Potassium (mmol/L)	Visit 1	267	4.4 (0.3)	200	4.4 (0.4)
	Visit 2	254	4.5 (0.4)	193	4.3 (0.4)
	Visit 3	247	4.4 (0.4)	192	4.2 (0.4)
	Visit 5	233	4.4 (0.4)	186	4.2 (0.4)
eGFR (ml/min/1.73m^2)	Visit 1	267	91.5 (15.8)	200	89.0 (15.1)
	Visit 5	234	90.9 (15.3)	187	86.6 (16.1)

2. Summaries of Heamatology Laboratory Assessments at visit 1 and visit 5 in Amlessa Arm and Co-Amlessa Arm in FAS

		Amlessa Arm		Co-Amlessa Arm	
		n	**Mean (SD)**	***n***	**Mean (SD)**
WBC (10^9/L)	Visit 1	253	7.4 (1.9)	193	7.3 (1.6)
	Visit 5	232	7.2 (1.9)	185	7.5 (1.8)
RBC (10^{12}/L)	Visit 1	253	5.0 (0.4)	193	5.0 (0.5)
	Visit 5	232	4.9 (0.4)	185	4.8 (0.4)
Hemoglobin (g/L)	Visit 1	253	149.4 (12.6)	193	147.7 (14.8)
	Visit 5	232	145.6 (11.5)	185	143.5 (13.7)
Hematocrit (L/L)	Visit 1	253	0.441 (0.037)	193	0.439 (0.042)
	Visit 5	232	0.431 (0.034)	185	0.424 (0.038)
MCV (fL)	Visit 1	253	88.8 (4.6)	193	88.3 (5.5)
	Visit 5	232	88.4 (4.6)	185	88.3 (5.0)
Platelets (10^9/L)	Visit 1	253	245.6 (56.4)	193	245.4 (57.8)
	Visit 5	232	249.4 (56.8)	185	251.4 (62.7)

Conclusions:

The results of the PRECIOUS study demonstrate that the treatment strategies with Amlessa and Co-Amlessa, tested in this study, result in effective reduction of office BP and lead to high rates of office BP target achievement after four months of treatment. Favourable results in office BP target achievement and reductions are further supported by clinically significant decrease in 24h BP observed in this study. Office BP decreased significantly within one month in both treatment arms and meaningful proportions of patients have achieved BP control after 1 month of treatment. The pattern of safety information in this study largely matched the established safety profile of the tested SPCs and the individual active substances, indicating good tolerability of the tested medications.

Results of clinical trial PRECIOUS provide additional support to the strategy of starting the antihypertensive treatment with a SPC in newly diagnosed patients and the strategy of intensifying the therapy in case of uncontrolled hypertension. Taking into consideration the findings of this study, it can be concluded that Amlessa and Co-Amlessa treatment strategies represent a useful tool for improving BP control in wide populations of patients, not only in significantly decreasing the office BP, but also the 24-hour BP parameters; thus widening the possibility of a comprehensive hypertension management.

Document Date:

16 October 2020