STATISTICAL ANALYSIS PLAN

Medivir AB

Protocol MIV-711-202

An Open-Label, One-Arm Phase II Extension Study to Evaluate Safety and Tolerability of MIV-711 in Patients with Knee Joint Osteoarthritis

PAREXEL Study Number: 230610

Final 1.0
Date: 16 January 2018

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Declaration

The undersigned agree to the statistical analyses and procedures of this clinical study.

16-JAN-2018

John Öhd
MD PhD
Chief Medical Officer
Medivir AB

Date (dd mmm yyyy)

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Delaration

The undersigned agree to the statistical analyses and procedures of this clinical study.

Heber, Walter

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Abbreviations and definitions

AE	Adverse event
BLQ	Below the lower limit of quantification
BMI	Body Mass Index
BML	Bone Marrow Lesions
CI	Confidence interval
CS	Clinically significant
CV	Coefficient of variation
DMC	Data monitoring committe
ECG	Electrocardiogram
FAS	Full analysis set
h	Hour
IMP	Investigational Medicinal Product
LLOQ	Lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
MOAKS	MRI Osteoarthritis Knee Score
NCS	Not clinically significant
NRS	Numeric Rating Scale
NK	Not known
OA	Osteoarthritis
PK	Pharmacokinetic
PPS	Per Protocol Set
q.d.	Once a day
QOL	Quality of Life
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard deviation
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
TIC	Time Integrated Concentrations
WHO-DD	World Health Organisation - Drug Dictionary

1. Statistical Analysis Plan

This Statistical Analysis Plan (SAP) provides a detailed and technical description of the planned statistical evaluation of the Medivir study MIV-711-202: "An Open-Label, One-Arm Phase II Extension Study to Evaluate Safety and Tolerability of MIV-711 in Patients with Knee Joint Osteoarthritis". The SAP also outlines the statistical programming specifications for the tables, listings and figures.

Full description of the investigational plan, selection criteria, assessments, etc. are given in the Clinical Study Protocol (CSP): MIV-711-202, dated 01 July 2016.

The planned analyses will be conducted by PAREXEL.

2. Study Objectives and Hypotheses

2.1 Primary Objective Study Group A

To assess the safety and tolerability of 200 mg MIV-711 q.d. over 52 (26+26) weeks in patients with symptomatic and radiographic knee osteoarthritis.

- Study Group A will be recruited from patients treated with 200 mg MIV-711 q.d. in Study MIV-711-201 and whose symptoms did not clinically significantly deteriorate as defined by an increase in NRS of ≤2 compared to Baseline.

2.2 Secondary Objectives Study Group A

To assess, in patients with symptomatic and radiographic knee OA, over 52 (26+26) weeks:

- The effect of MIV-711 on MRI cartilage thickness loss
- The effect of MIV-711 on MRI bone marrow lesion volume
- The effect of MIV-711 in the semi quantitative MRI Osteoarthritis Knee Score (MOAKS) parameters
- To assess the effect of MIV-711 on MRI knee joint bone area.

Note: all MRI assessments refer to the target knee unless stated otherwise.
Target knee is identified by knee pain on a numeric rating scale and Kellgren and Lawrence classification grade. If patients have knee pain in both sides with equal regard to these two criteria, the right knee should always be prioritized. The target knee in Study MIV-711-202 must be the same as in Study MIV-711-201.

2.3 Secondary Objectives Study Group B

To assess the effect of 200 mg MIV-711 q.d. on safety and tolerability over 26 weeks in patients with symptomatic and radiographic knee osteoarthritis.

- Study Group B will be recruited from patients receiving placebo in Study MIV-711-201 having experienced a clinical worsening as defined by an increase in NRS of ≥2 versus Baseline.
- Data from both MIV-711-201 and MIV-711-202 studies will be used for Group B assessment

2.4 Exploratory Objectives Study Group A

Data from both MIV-711-201 and MIV-711-202 study will be used for Group A assessment.

In addition, the study will investigate the following exploratory parameters.

- The effect of MIV-711 on worst target knee pain (1 week recall)
- The effect of MIV-711 on average contralateral knee pain (1 week recall)
- The effect of MIV-711 on constant and intermittent OA pain
- The effect of MIV-711 on global improvements in knee problem, knee pain and knee function
- The effect of MIV-711 on knee joint OA symptoms (function, pain, stiffness)
- The effect of MIV-711 on global disease activity
- The effect of MIV-711 on quality of life (QoL)
- The effect of MIV-711 on patient reported e-diary daily recall knee joint pain
- The effect of MIV-711 on patient reported e-diary daily recall analgesics use
- Assessment of the effect of MIV-711 on exploratory serum and urinary biomarkers of relevance for OA including but not limited to procollagen type I N-terminal propeptide (PINP), bone specific alkaline phosphatase (BSAP), N-terminal telopeptide of collagen type I (NTX-I), CTX-I, aCTX-I, CTX-II and tartrate-resistant acid phosphatases (TRAP5b).
- Baseline and steady state treatment blood and urinary samples will be stored for patients who sign a separate voluntary Informed Consent Form (ICF) for potential future pharmacogenomics and disease-related proteomics, genomics, metabolomics and lipidomics analyses.
- The effect of MIV-711 on a compound index of MRI bone area and cartilage thickness
- The pharmacokinetics of MIV-711 and the relationship to patient actors and concomitant medications

2.5 Exploratory Objectives Study Group B

All of the above noted secondary and exploratory parameters described in Section 2.2 and Section 2.4 for study group A, are considered as exploratory objectives in study group B and will be evaluated over 26 weeks on 200 mg MIV-711 succeeding 26 weeks on Placebo.

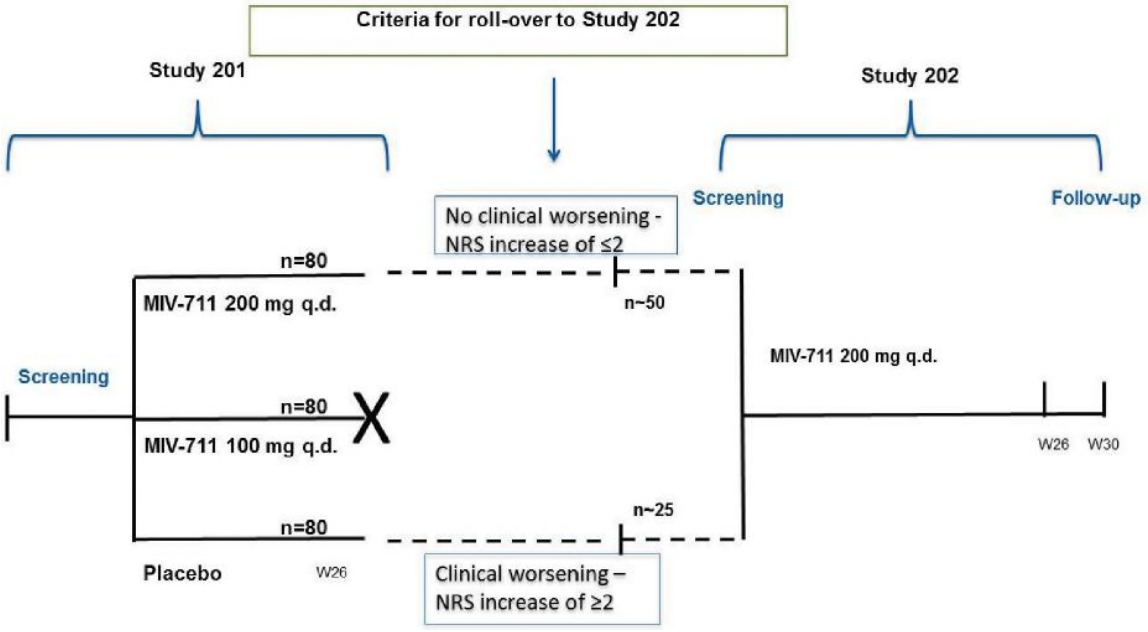
3. Study Design

This study is a 6-month open-label one-arm extension study evaluating safety and tolerability as well as the efficacy of 200 mg MIV-711 q.d. in two separate patient populations denoted as study Group A and Group B.

Study Group A patients will be recruited from Study MIV-711-201 who were treated with 200 mg MIV-711 q.d. and whose symptoms did not clinically significantly deteriorate as defined by an increase in the numeric rating scale (NRS) of ≤2 compared to Baseline. Patients eligible for Study Group A will be offered 6 months' extended treatment, primarily evaluating longer term safety and tolerability. The total treatment duration of 52 weeks also allows a more suitable treatment length for the exploratory study of any structural effects of MIV-711 on joint cartilage thickness.

A further rationale of this study is to explore the treatment effect in a group of OA patients that have confirmed symptom progression over the last 6 months (Study Group B). Study Group B will be recruited from patients receiving placebo in Study MIV-711-201 who experienced a clinical worsening as defined by an increase in NRS of ≥2 versus Baseline. Patients eligible for Study Group B will be offered 200 mg MIV-711 q.d. for the next 26 weeks. In addition to offering the treatment to appropriate patients, this also enables the assessment of the effects of MIV-711 based on MRI imaging, symptoms and biomarkers in patients with progressing symptoms and, as such, has the potential to provide valuable information for future patient selection in OA trials. Similar to Study MIV-711-201, the joint structural endpoint of choice over 6 months treatment constitutes MRI joint bone surface measurement. All analyses, with the exception of safety and tolerability, will be conducted as exploratory with regards to Study Group B.

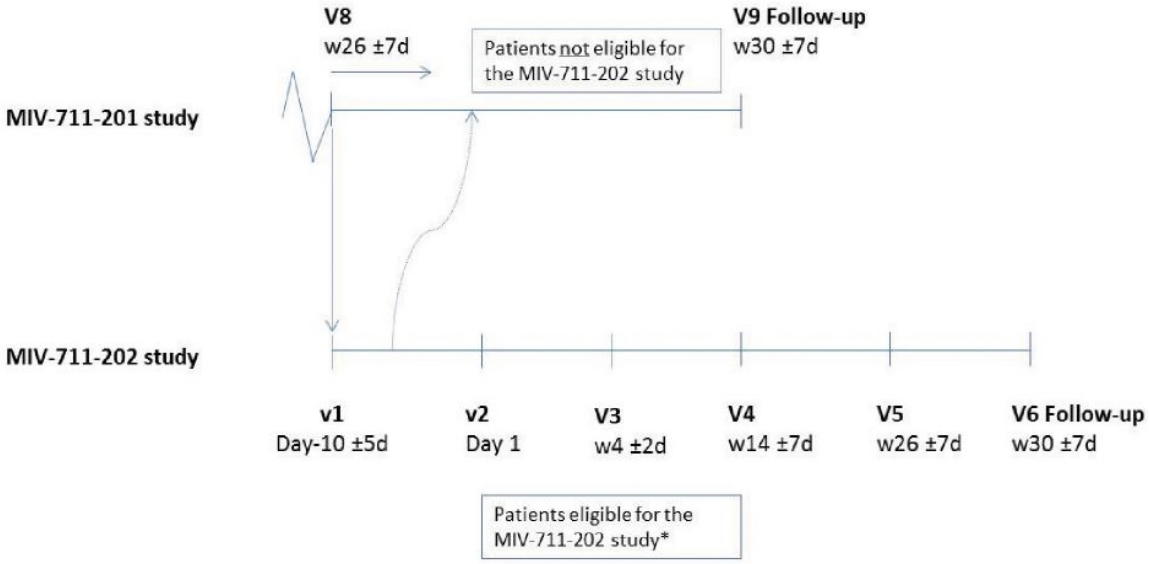
The analysis of data from this study will not be based on a formal statistical analysis since the primary endpoint constitutes safety and tolerability.



The study consists of a Screening period of approximately 2 weeks (Visit 1), eligibility at Visit 2, an open-label treatment period of 26 weeks from Visit 2 through Visit 5, and a follow-up period of 4 weeks (Visit 6) after the last dose of study treatment is administered. Telephone calls will be made 5-9 days after all dosing visits for safety and tolerability. There will be additional phone calls at Week 10 and Week 20 for safety and tolerability.

A Data Monitoring Committee (DMC) will meet to review the safety and tolerability data after the first 25 patients complete Visit 4 and Visit 5.

The study design is summarized in the figure below.



*) Patients eligible for the MIV-711-202 study will not do the follow up visit in the MIV-711-201 study but the corresponding visit in the MIV-711-202 study.

3.1 Study Population

The study population will consist of patients with symptomatic and radiographic knee joint OA who have participated in Study MIV-711-201. Patients must be able to provide written consent and meet all the inclusion criteria and none of the exclusion criteria.

3.2 Recruitment, Planned Sample Size and Number of Study Centres

The roll-over of individual patients to Study MIV-711-202 is based on the criteria for study Groups A and B detailed above and is executed by a central person independent from the study with access to the randomisation list and eCRF for Study MIV-711-201. Based on a selection criteria for study Group A and B described earlier in this section, it is anticipated that 50-80 patients will be eligible for participation. Recruitment may be terminated if considered appropriate or necessary by the sponsor.

3.3 Patient Withdrawal and Replacement

In order to perform the intent to treat (ITT) analysis, and to enable safety analyses, all patients who discontinue their randomised medication will be asked to still complete their follow-up visit (visit 6) as outlined in the study schedule. An MRI scan should be completed if withdrawal is after Visit 4. This MRI is only done as a safety parameter and is not to be included in any endpoint analysis.

Patients who withdraw from the study will not be replaced.

Other reasons a patient maybe removed from the study are outlined in Section 5.3 in the protocol.

3.4 Patient Identification

3.4.1 Patient Identification

The Principal Investigator or qualified designee will obtain signed, informed consent from the potential study patient before any study-specific procedures are performed.

After written informed consent has been obtained, each patient will receive a unique patient number.

The patient number allocated to any patient will not be reallocated to other patients if he/she terminates the study participation for any reason, regardless of whether IMP was taken or not.

3.4.2 Allocation of Patients to Treatment

This is an open label study and all patients will receive 200 mg q.d. The first dose of IMP will be administered at Visit 2 (Enrolment) after the patient has signed the informed consent form and the Investigator has confirmed the patient's eligibility based on screening procedures performed.

3.5 Study Drug Administration

In Study MIV-711-202, all patients will receive 200 mg q.d. oral dose of MIV-711 for 26 weeks. The IMP should be taken q.d. in the morning approximately 24 hours apart. The first dose in Study MIV-711-202 is administered at the site during Visit 2 (Enrolment). All patients must stay at the site 2 hours after administration of the first dose.

IMP should be dispensed during the Visits 2 and 4 and returned by the patients for drug accountability at Visit 4 and Visit 5.

On days when the patient is visiting the site the IMP must be taken at the site under fasting conditions (and not at home) and the time of the intake must be recorded in the source documents.

3.6 Interim Analysis

No interim analysis will be conducted for any efficacy endpoint. Interim safety data will be reviewed during DMC meetings after the first 25 patients have completed Visit 4 and Visit 5. No formal statistical tests will be undertaken. Adverse events will be summarised descriptively and tabulated for all patients by treatment group. The DMC will consider the results of the AE summaries when making decisions regarding dosing of subsequent cohorts (i.e. need for dose stoppages) or the need for formal interim analysis of non-safety data.

4. Study Analysis Variables

The study variables are collected for the two studies MIV-711-201 and MIV-711-202 according to the study schedules displayed in section 4.1 and section 4.2, respectively.

4.1 Study Schedule MIV-711-201

Study Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9
Weeks	-4	1	2	4	8	14	20	26	30
Day	up to 30 days	Day 1	day 15 ±2 days	day 29 ±2 days	day 57 ±2 days	±7 days	±7 days	±7 days	± 7 days
Visit Description	Screening	Randomisation/ Baseline	Treatment period						Safety follow- up
Signed informed consent	X								
Randomisation		X							
Inclusion/exclusion criteria	X	X							
Target knee identification[A]	X								
Demographics	X								
Weight	X							X	
Height	X								
Medical & Surgical history	X								
Physical examination	X	X	X[B]	X[B]	X	X	X[B]	X	
Vital signs, including body temperature	X	X	X	X	X	X	X	X	X
12-Lead ECG[C]	X	X	X	X	X	X	X	X	X

Study Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9
Weeks	-4	1	2	4	8	14	20	26	30
Day	up to 30 days	Day 1	day 15 ±2 days	day 29 ±2 days	day 57 ±2 days	±7 days	±7 days	±7 days	± 7 days
Visit Description	Screening	Randomisation/ Baseline	Treatment period						Safety follow- up
Clinical chemistry/ Haematology	X	X	X	X	X	X	X	X	X
Urinalysis[D]	X	X	X	X	X	X	X	X	X
Urine drug screen	X				X				
Post-menopausal assessment (females only)	X								
HBsAg, anti-HBc, anti-HBs, HCV, and HIV test	X								
e-diary dispensing and training	X								
Patient Emergency Card dispense	X								
MRI of target knee[E]		X						X	
e-diary for pain and analgesic[F]		X				X		X	
Duration and onset of knee pain		X							
NRS, ICOAP, WOMAC	X[G]	X			X	X		X	X[G]

Study Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9
Weeks	-4	1	2	4	8	14	20	26	30
Day	up to 30 days	Day 1	day 15 ±2 days	day 29 ±2 days	day 57 ±2 days	±7 days	±7 days	±7 days	± 7 days
Visit Description	Screening	Randomisation/ Baseline	Treatment period						Safety follow- up
Global improvement (6-point Likert scale)					X	X		X	
EuroQoL EQ-5D-5L		X						X	
Brief Medication Questionnaire					X	X		X	
Dispense IMP[I]		X[H]			X	X			
Drug accountability		X			X	X		X	
PK sampling (blood)				X				X	
Biomarker samples[J]		X		X		X		X	X
AEs/SAEs monitoring	X	X	X	X	X	X	X	X	X
Concomitant Medication		X	X	X	X	X	X	X	X
Phone call to assess safety and tolerability[K]		X	X	X	X	X	X		
Blood sample for pharmacogenomics, proteomics, genomics, metabolomics and lipidomics and urine sample for proteomics and metabolomics[L]		X						X	

Abbreviations: AE=Adverse event; anti-HBc=Total Hepatitis B core antibody; anti-HBs= Antibody to Hepatitis B surface antigen; ECG=Electrocardiogram; eCRF=Electronic case report form; EQ-5D-5L=EQ-5D is a standard measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal; HBsAg=Hepatitis B surface antigen; HCV=Hepatitis C virus; HIV=Human immunodeficiency virus; ICOAP=Intermittent and constant osteoarthritis pain; IMP=Investigation medicinal product; K-L=Kellgren and Lawrence; MRI=Magnetic resonance imaging; NRS=Numeric rating scale; PK=pharmacokinetic(s); PRO=Patient reported outcomes; SAE=Serious adverse event; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.

A. Selection of target knee was to be primarily based on pain, secondarily on K-L Grade, and if both sides were equal with regard to these two criteria, the right knee was always to be prioritised.
B. Targeted physical examination. Full physical examination at all other visits.
C. At Visit 2 at pre-dosing, 0.5, 1 and 2 hours post-dosing (± 10 minutes). At all other visits 30 minutes post-dose (± 10 minutes).
D. If urinalysis was positive for blood, nitrites, leukocyte esterase, and/or protein, additional microscopic analysis was to be performed.
E. MRI was to be performed at Visit 2 (-7 days) and at Visit 8 (± 5 days).
F. To be completed at home during the 2 weeks prior to the marked visit.
G. Only NRS for average overall knee pain severity (1-week recall) for both knees.
H. The first dose of IMP was to be dispensed to the patient at the site. Date and time was to be recorded in the eCRF. The first dose was to be given to the patient after all baseline assessments had been performed including completion of Patient Reported Outcomes (PROs). Patients were to take the IMP in the clinic in a fasting state and were required to stay at the clinic for 2 hours after intake of the IMP.
I. Patients were to take the IMP in the clinic in a fasting state. Breakfast was to be eaten 1 hour after IMP intake. The last dose of the IMP was to be taken at the site during Visit 8.
J. Both blood and urine samples were to be collected for biomarker. The first void of morning urine must have occurred before the urine sample was taken from a later void. The patients were to be fasting when all biomarker samples were taken.
K. The phone call was to be made 5-9 days after all dosing visits.
L. Blood was to be collected for pharmacogenomics, proteomics, genomics, metabolomics and lipidomics and urine was to be collected for proteomics and metabolomics pre-dose at Visit 2 (baseline) and Visit 8 from patients who provided additional written.

4.2 Study Schedule MIV-711-202

Study Visit	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**
Weeks	**-2**	**1**	**4 ±2 days**	**14 ±7 days**	**26 ± 7 days**	**30 ± 7 days**
Day	**-10 ± 5 days**	**Day 1**	**28 ±2 days**	**98 ±7 days**	**182 ± 7 days**	**210 ± 7 days**
Visit Description	**Screening[A]**	**Enrolment**	**Safety**	**Safety and Treatment**		**Safety follow-up**
Signed informed consent	X	X[B]				
Inclusion/exclusion criteria	X	X				
Demographics	X					
Weight	X					
Medical & Surgical history	X					
Physical examination	X[C]	X	X	X	X	
Vital signs, including body temperature	X[C]	X	X	X	X	X
12-Lead ECG[D]	X[C]	X[E]	X	X	X	X
Clinical chemistry/Haematology	X[C]	X	X	X	X	X
Urinalysis[F]	X[C]	X	X	X	X	X
Urine drug screen	X					
Post-menopausal assessment (females only)	X					
e-diary dispensing and training		X				

Study Visit	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**
Weeks	**-2**	**1**	**4 ±2 days**	**14 ±7 days**	**26 ± 7 days**	**30 ± 7 days**
Day	**-10 ± 5 days**	**Day 1**	**28 ±2 days**	**98 ±7 days**	**182 ± 7 days**	**210 ± 7 days**
Visit Description	**Screening[A]**	**Enrolment**	**Safety**	**Safety and Treatment**		**Safety follow-up**
e-diary for pain and analgesic[G]				X	X	
Patient Emergency Card Dispensing	X					
MRI of the bone area					X[H]	
Registration in the IWRS	X					
NRS, ICOAP, WOMAC				X	X	
Global improvement (6-point Likert scale)				X	X	
EuroQoL EQ-5D-5L					X	
Brief Medication Questionnaire				X	X	
Dispense IMP[I]		X[J]		X		
Drug accountability				X	X	
e-diary return					X	
PK sampling (blood)					X	
Biomarker samples[K]		X		X	X	X
AEs/SAEs monitoring	X	X	X	X	X	X

Study Visit	V1	V2	V3	V4	V5	V6
Weeks	**-2**	**1**	**4 ±2 days**	**14 ±7 days**	**26 ± 7 days**	**30 ± 7 days**
Day	**-10 ± 5 days**	**Day 1**	**28 ±2 days**	**98 ±7 days**	**182 ± 7 days**	**210 ± 7 days**
Visit Description	**Screening[A]**	**Enrolment**	**Safety**	**Safety and Treatment**		**Safety follow-up**
Concomitant Medication		X	X	X	X	X
Phone call to assess safety and tolerability[L]		X	X	X	X	
Blood sample for pharmacogenomics, proteomics, genomics, metabolomics and lipidomics and urine sample for proteomics and metabolomics					X[M]	

Abbreviations: AE=adverse event; ECG=electrocardiogram; eCRF=electronic case report form; DNA=deoxyribose nucleic acid; EuroQoL EQ-5D-5L= a standard measure of health status developed by the EuroQol Group in order to provide a simple, generic measure of health for clinical and economic appraisal; FSH=follicle stimulating hormone; ICF=informed consent form; ICOAP=intermittent and constant osteoarthritis pain; IMP=investigational medicinal product; IWRS= Interactive Web Response System; MRI=magnetic resonance imaging; NRS=numeric rating scale; PK=pharmacokinetic; PRO=patient-reported outcomes; RNA=ribonucleic acid; SAE=serious adverse event; WOMAC= Western Ontario and McMaster Universities Osteoarthritis Index

A) The Screening visit (Visit 1) will coincide with 26-week End of Treatment visit of Study MIV-711-201 (Visit 8).
B) Optional ICF to be provided and signed at Visit 2.
C) Assessed at Visit 8 in Study MIV-711-201. Only need to be re-assessed if Visit 8 does not occur on the same day as Visit 1 in Study MIV-711-202
D) 30 minutes post-dose (± 10 minutes).
E) 12-lead serial ECGs will be recorded at Visit 2 (Enrolment) pre-dosing and after 30 minutes, 1 hour and 2 hours post-dosing (± 10 minutes).
F) If urinalysis is positive for blood, nitrites, leukocyte esterase, and/or protein, additional microscopic analysis may be performed.
G) To be completed at home during the 2 weeks leading up to the marked visit with final recording the day before.
H) ± 5 days
I) Patients take IMP in the clinic in a fasting state. Breakfast can be eaten 1 hour after IMP intake. The last dose of the IMP will be taken at the site during Visit 5.
J) The first dose of IMP will be dispensed to the patient at the site and the patient must stay at the clinic for 2 hours after intake of IMP. Date and time should be recorded in the

Study Visit	V1	V2	V3	V4	V5	V6
Weeks	-2	1	4 ±2 days	14 ±7 days	26 ± 7 days	30 ± 7 days
Day	-10 ± 5 days	Day 1	28 ±2 days	98 ±7 days	182 ± 7 days	210 ± 7 days
Visit Description	Screening[A]	Enrolment	Safety	Safety and Treatment		Safety follow-up

eCRF. The first dose should be given to the patient after all assessments at Enrolment have been performed.

K) Both blood and urine sample will be collected for biomarkers. The first void of morning urine should have occurred before the urine sample is taken from a later void. The patients must be fasting when all biomarker samples are taken.

L) The phone call should be made 5-9 days after all dosing visits. There will be additional phone calls at Week 10 and Week 20.

M) Blood will be collected for pharmacogenomics, proteomics, genomics, metabolomics and lipidomics and urine will be collected for proteomics and metabolomics pre-dose at Visit 5 from patients who provide additional written consent.

4.3 Demographic and Background Variables

The following demographic and anthropometric information will be recorded at screening:

- Date of informed consent
- Medical and surgical history (including previous and current medical conditions and medications)
- Age calculated as (date of informed consent – date of birth)/365.25
- Gender
- Ethnic origin
- Race
- Height (cm)
- Body weight (kg)
- Body mass index (BMI) (kg/m^2)

Adverse Events from MIV-711-201 will be recorded as Medical history in MIV-711-202.

Concomitant medication in MIV-711-201 will be recorded as prior medication in MIV-711-202.

4.4 Safety Variables

4.4.1 Adverse Events

All AEs and SAEs will be recorded in the eCRF system from the date the informed consent form is signed (visit 1) until the safety follow up visit (visit 6) is completed.

4.4.2 Clinical Laboratory Tests

Blood samples for hematology and clinical chemistry, and urinalysis assessments will be collected during all study visits: Visit 1 (screening), Visit 2 (Week 1), Visit 3 (Week 4), Visit 4 (Week 14), Visit 5 (Week 26), Visit 6 (Week 30, follow-up).

The following safety laboratory parameters will be measured:

Hematology: WBC and differential, % and absolute for: neutrophils, lymphocytes, monocytes, eosinophils, basophils; hemoglobin, hematocrit, RBC, RBC indices (MCV, MCH and MCHC) and morphology, platelet count

Chemistry: urea nitrogen, creatinine, calcium, sodium, potassium, bicarbonate, chloride, total protein, fasting glucose, total bilirubin, direct bilirubin and indirect bilirubin, ALT, AST, alkaline phosphatase, GGT, CPK, CRP.

Urinalysis: with microscopic: specific gravity, pH, protein, glucose, ketones, nitrites, blood and leukocyte esterase

4.4.3 Other Laboratory Tests

- Post-menopausal determination at Visit 1 (screening): Follicle stimulation hormone (FSH) in female patients.
- Urine Drug Screen measured at screening and Visit 1 (Screening): Amphetamine, Benzodiazepines, THC, Cocaine, Oxycodone and Opiate.
- PTH (parathyroid hormone)

4.4.4 Vital Signs

Vital signs (body temperature, heart rate, blood pressure, oxygen saturation) will be performed at all clinic visits prior to IMP dosing: Visit 1 (screening), Visit 2 (Week 1), Visit 3 (Week 4), Visit 4 (Week 14), Visit 5 (Week 26), Visit 6 (Week 30), safety follow up. All assessments will be collected in the supine position.

Weight will be measured at visit 1 (screening).

4.4.5 Electrocardiograms

A 12-lead ECG will be performed at all clinic visits. 12-lead serial ECGs will be recorded at visit 2 (enrolment) pre-dosing and after 30 minutes, 1 hour and 2 hours post-dosing (± 10 minutes).

The clinical significance of ECG results will be determined by the investigator after review of the ECG report in relation to the patient‘s medical history, physical examination findings, and concomitant medications.

4.4.6 Physical Examination

A standard complete physical examination will be performed at Visit 1 (Screening), Visit 2 (Enrolment), Visit 3, Visit 4 and Visit 5.

4.4.7 Prior and Concomitant Medications

All prior and concomitant medications taken during the MIV-711-202 study will be recorded with generic name, indication, daily dose, and start and stop dates of administration at each visit. For this study, prescription medicines, other than those prohibited by the study protocol are permitted as concomitant medications to manage ongoing or chronic, stable medical conditions. Concomitant medications from the MIV-711-201 study that were taken prior to visit 2 in the MIV-711-202 study are captured as prior medications in the current study. Any change in prior medications past visit 2 IMP administration in MIV-711-202, or any new medications, are documented as concomitant medication. All patients will be asked about concomitant medication use and any changes to use of concomitant medications at all study visits. Patients will be permitted to reinstate prohibited concomitant medications on completion of their follow up study visit.

The Brief Medication Questionnaire self-reported measure for the use of concomitant medication will be included at visit 4 and visit 5.

4.4.8 Phone Call to Assess Safety and Tolerability

Follow-up telephone calls to assess safety and tolerability will occur 5 to 9 days after visit 2, visit 3 and visit 4. There will be additional phone calls at Week 10 and Week 20 for safety and tolerability.

4.5 Efficacy Variables

4.5.1 MRI Bone Shape Modelling by Imorphics

MRIs will be analysed quantitatively using statistical shape modelling (SSM, Imorphics Ltd).

Bone shape modelling of MRI by Imorphics will be used to assess:

- Mean cartilage thickness (mm) for each of the anterior, posterior and central regions, with areas denuded of cartilage included as having zero thickness
- Bone marrow lesion volume (mm3) by anatomical region: medial and lateral femorotibial region of femur, medial and lateral pate llofemoral region of femur, medial and lateral tibia, and patella
- Bone area (mm2) for anatomical regions: lateral and medial femur (patellofemoral); lateral and medial femur (femorotibial); lateral and medial patella, lateral and medial tibial condyle
- Bone shape by distance along an OA shape vector for femur, tibia and patella
- Index bone area/cartilage thickness

Below are the denominations of the data items provided by Imorphics that will provide the basis for bone area and cartilage thickness and bone marrow lesion volume.

- MF_TAB: Area of bone in the medial femur region, MF
- CM_FEMUR_THCTAB: Average thickness of cartilage in the central medial femur region
- CM_TIBIA_THCTAB: Average thickness of cartilage in the central medial tibia region
- TOTAL_BML_VOLUME: Combined volume of all BML regions

4.5.2 MRI MOAKS

MRIs will be analysed semi-quantitatively by a central musculoskeletal radiologist using the MOAKS.

MOAKS scoring will be used to assess the following features:

- Bone marrow lesions (BMLs) and cysts
- Articular cartilage
- Osteophytes

MRI assessment using MOAKS scoring will be used to assess the following features, as provided by PAREXEL MRI:

- Bone Marrow Lesions (BMLs) and cysts. This involves 15 subregions graded for BML size (including ill-defined lesion and cysts) measuring the total volume of the subregion occupied by BML(s). Grade 0= none, grade 1 < 33% of subregional volume, grade 2 = 33 to 66% of subregional volume and grade 3 > 66% of subregional volume.

- Articular Cartilage: This involves 14 articular cartilage regions graded for size of any cartilage loss (including partial and full thickness loss) as a percentage of surface area as related to the size of each individual region surface and percentage of loss in this subregion that is full-thickness loss.

- Osteophytes: This involves 12 sites scored for presence and size of osteophytes. Grade 0=none, Grade 1= small, Grade 2 = medium, Grade 3 = large.

The specific subregions associated with the above three groups of MOAKS scoring are outlined in the table below:

Bone Marrow Lesions (BMLs) and cysts	Articular Cartilage	Osteophytes
Medial Patella	Medial Patella	Superior Patella
Lateral Patella	Lateral Patella	Inferior Patella
Medial Femur Trochlea	Medial Femur Trochlea	Medial Patella

Medial Femur Central	Medial Femur Central	Lateral Patella
Medial Femur Posterior	Medial Femur Posterior	Medial Femur Trochlea
Lateral Femur Trochlea	Lateral Femur Trochlea	Medial Femur Central
Lateral Femur Central	Lateral Femur Central	Medial Femur Posterior
Lateral Femur Posterior	Lateral Femur Posterior	Lateral Femur Trochlea
Medial Tibia Anterior	Medial Tibia Anterior	Lateral Femur Central
Medial Tibia Central	Medial Tibia Central	Lateral Femur Posterior
Medial Tibia Posterior	Medial Tibia Posterior	Tibia Medial
Subspinous	Lateral Tibia Anterior	Tibia Lateral
Lateral Tibia Anterior	Lateral Tibia Central	
Lateral Tibia Central	Lateral Tibia Posterior	
Lateral Tibia Posterior		

Bone Marrow Lesions (BMLs) and cysts: The 15 subregions will be assessed for:

- Size of BML
- Number of BMLs
- Percentage that is BML

Articular Cartilage: The 14 subregions will be assessed for:

- Size of any cartilage loss
- Percentage of Full Thickness Loss

4.5.3 Patient Reported Outcomes (PROs)

At Visit 4 and 5 the following PROs will be recorded using questionnaires as specified in the schedule of assments (see Protocol Table 2).

- Average overall knee pain severity in the target knee over the past 1 week (0-10 NRS)
- Worst knee pain severity in the target knee over the past 1 week (0-10 NRS)
- Global disease activity over the past 1 week (0-10 NRS)
- Average overall knee pain severity in the contralateral knee over the past 1 week (0-10 NRS)
- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Higher scores indicate worse pain, stiffness and physical function. The subscale scores are derived by summing the assigned values on component items. The study joint referred in the WOMAC questionnaire corresponds to the target knee (as referenced elsewhere in this protocol).
- Osteoarthritis Research Society International (OARSI)-OMERACT Responder index will be calculated using the WOMAC pain and function subscales and the patient's global assessment score.

- Intermittent and constant osteoarthritis pain (ICOAP) - an 11-item tool designed to assess constant and intermittent OA pain. The tool will be self-reported. (The tool was designed for telephone or interview administration but self-reporting is allowed.) The questions will be scored according to a user manual into a constant pain subscale, intermittent pain subscale and total pain score. These scores will be transformed to a 0-100 scale for analysis.
- Global improvements in knee problem, knee pain and knee function recorded on a 6-point Likert scale: completely better, much better, better, no change, worse, much worse.

- EuroQol-5 Dimensions (EQ-5D-5L) (Visit 5 only) - a generic measure of self-reported health status that defines health status in terms of five dimensions – mobility; self-care; usual activity; pain or discomfort; and anxiety or depression

- In an e-diary format, a patient knee pain diary (NRS) and analgesia questionnaire will be completed daily during two 2-week periods prior to Visit 4 and Visit 5. Baseline (Visit 8 of Study MIV-711-201) will be defined as the last observation prior to the first dose of investigational product. The assessments in the e-diary comprise:

1) Average overall knee pain severity in the target knee over the past 12 hours (0-10 NRS)
2) Adherence to usual analgesics regimen

- Intake of IMP (only included with an attempt to improve compliance, no data to be reported)

4.5.3.1 NRS Score Descriptions

For the purposes of the questions below, the target knee is defined as the knee studied in this trial. Pain in the knee relates to any knee symptom the patient may experience for example pain or aching.

The scale ranges for NRS pain scores range from 0 indicating —"no pain", to 10 indicating —"pain as bad as it could be". The NRS scales will be used to assess for:

1) NRS question 1: NRSPTO. On average, how would you rate the overall pain severity in your target knee over the last week (7 days)?

2) NRS question 2: NRSPAINW. How would you rate your worst pain severity in your target knee over the last week (7 days)?

3) NRS question 3: NRSPAINS. On average, how would you rate the overall pain severity in your other knee over the last week (7 days)?

4) NRS question 4: NRSACT. Over the last week (7 days), how active do you think your target knee arthritis has been?

5) NRS question 5: NRSSAT. Over the last week (7 days), how satisfied have you been with your target knee function?

For purposes of this SAP NRS question 4 refers to the patients "Global Assessment Score".

4.5.3.2 ICOAP Score Descriptions

Intermittent and constant osteoarthritis pain (ICOAP): an 11-item tool designed to assess constant and intermittent pain. Higher scores indicate worse constant and intermittent pain. The items assessed include:

- IP1- How intense has constant knee pain been
- IP2-Constant knee pain affecting sleep
- IP3-Constant knee pain - quality of life
- IP4-Frustrated by your constant knee pain
- IP5-Upset by your constant knee pain
- IP6-Intensity of pain that comes and goes
- IP7-Frequency pain that comes and goes
- IP8-Pain comes and goes affecting sleep
- IP9-Pain comes and goes quality of life
- IP10-Frustration pain that comes and goes
- IP11-Upset pain that comes and goes

4.5.3.3 WOMAC Score Descriptions

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) 3.1: a 24-item OA - specific, tri-dimensional self-administered questionnaire, for assessing health status and health outcomes in OA of the knee. Using an 11-box NRS scale, higher scores indicate worse pain, stiffness and physical function. Items assessed include:

- WOMAC1-Pain - walking on a flat surface
- WOMAC2-Pain - going up or down stairs
- WOMAC3-Pain - at night while in bed

- WOMAC4-Pain - sitting or lying down
- WOMAC5-Pain - while standing
- WOMAC6-Stiffness after first woke up in morning
- WOMAC7-Stiffness sitting or lying down
- WOMAC8-Difficulty - When going down the stairs
- WOMAC9-Difficulty - When going up the stairs
- WOMAC10-Difficulty - Getting up from a sitting
- WOMAC11-Difficulty - While standing
- WOMAC12-Difficulty - When bending to the floor
- WOMAC13-Difficulty - Walking on a flat surface
- WOMAC14-Difficulty - Getting in or out of a car
- WOMAC15-Difficulty - While going shopping
- WOMAC16-Difficulty - When putting on your socks
- WOMAC17-Difficulty - When getting out of bed
- WOMAC18-Difficulty - When taking off your socks
- WOMAC19-Difficulty - While lying in bed
- WOMAC20-Difficulty - Getting in or out of bath
- WOMAC21-Difficulty - While sitting
- WOMAC22-Difficulty - Getting on or off toilet
- WOMAC23-Difficulty - Performing heavy duties
- WOMAC24-Difficulty - Performing light duties

4.5.3.4 OARSI OMERACT Score Descriptions

OARSI-OMERACT Responder index [2, 3] will be calculated using the WOMAC pain and function subscales and the patient‘s global assessment score as described in sections 4.5.3.1 and 4.5.3.3. A responder will be defined as any subject that satisfies one of the following two overall conditions:

CASE 1. Improvement in pain or function ≥50% and absolute change ≥20

CASE 2. Improvement in at least two of the following conditions:
1. pain ≥20% and absolute change ≥10
2. function ≥20% and absolute change ≥10
3. patients‘ global assessment ≥20% and absolute change ≥10

Higher scores indicate worse pain, stiffness and physical function so that an “improvement” is only concerned with negative changes (or decreases) from baseline. Positive increases in scores relative to baseline suggest a worsening of pain (scores increasing over time suggests pain is increasing in severity over time).

4.5.3.5 Global Improvement Score Descriptions

Global improvements in knee problem, knee pain and knee function (Ability to use knee), recorded on a 6-point Likert scale at visit 4 and visit 5: (completely better, much better, better, no change, worse, much worse).

4.5.3.6 Quality of Life

At visit 5: EuroQol -5 Dimensions (EQ-5D-5L) - a generic measure of self-reported health status. Items assessed include:

- Usual Activities
- Anxiety/Depression
- Self-Care
- Pain/Discomfort
- Mobility
- Health Rating

4.5.3.7 Brief Medication Questionnaire

The Brief Medication Questionnaire is a self-reported measure for the use of concomitant medication and will be administered at visit 4 and visit 5. Items assessed include:

- How much did you take each time
- How many days did you take it
- The dosage times are inconvenient
- How many times per day did you take it
- It is hard to get my refill on time
- How many times did you miss taking it
- It is hard to open the container
- Hard to read the print on the container
- For what reason were you taking it
- It is hard to remember all doses
- Stop taking meds since the start of the study or since the previous visit
- Medication Name

4.5.3.8 E-Diary Assessment of NRS and Analgesic Use

In an e-diary format, a patient knee pain diary (NRS) and analgesia questionnaire will be completed daily every 12 hours (AM, PM) during two 2-week periods prior to visit 4 and visit 5. The assessments in the e-diary comprise:

- Average overall knee pain severity in the target knee over the past 12 h (0 -10 NRS)
- Adherence to usual analgesics regimen:
  - Has patient taken any pain medication over last 12 hours? (Yes, No).
  - Classify your pain medication usage over the last 12 hours: (More than normal, Normal, Less than normal)
- Intake of IMP (note: the e-diary device is kept by the patients for the full duration of the study, intake of IMP will be registered daily throughout the study)

4.5.4 Other Efficacy Parameters – Biomarkers, Imaging, Pharmacokinetics

Biomarkers

Blood and urine samples will be taken at Visits 2, 4, 5 and 6, for analysis of exploratory bone and cartilage markers of relevance for OA disease, such as CTX-I, PINP, BSAP and TRAP5b in serum and NTX-I, CTX-I, alphaCTX-I and CTX-II in urine.

Imaging

The imaging assessment will be derived in the source as change from baseline to Visit 5 in the current study as a calculated compound index of MRI bone area and cartilage thickness.

Pharmacokinetics

The analysis of the pharmacokinetics and metabolism of MIV-711 and the relationship to patient factors and concomitant medications will be conducted by the sponsor and described in a separate report. The PK analysis will not be considered in this SAP.

4.6 Analysis Populations

The analysis populations that will be used in the analyses are defined in Section 4.6.1, Section 4.6.2 and Section 4.6.3 below. Note that the analysis populations Population A and Population B as defined in the CSP are not considered statistical analysis populations but defined to indicate the two different treatment groups. No amendment to the CSP will be done, but the discrepancy between the CSP and the SAP regarding the analysis populations will be clarified in the section “Changes to planned analysis” in the CSR.

4.6.1 Intent-to-Treat Population (ITT)

All patients enrolled to the study MIV-711-202 and recieves at least one dose of the IMP.

4.6.2 Per Protocol Population (PPS)

The patients in the ITT population without any major protocol deviations as described in section 5. A patient that discontinuates from the study will typically be part of the ITT population but will not be included in the PPS population.

4.6.3 Safety Analysis Population (SAF)

The safety analysis population will be the same as the ITT population.

5. Protocol Deviations

Deviations from the protocol including violations of inclusion/exclusion criteria will be assessed as “minor” or “major” in cooperation with the sponsor. Major deviations from the protocol will lead to the exclusion of a patient from the Per Protocol Set (PPS). Deviations will be defined prior to data base hard lock.

The following criteria will be used to exclude a patient from an analysis set:

- Incorrect diagnosis
- Any of the prohibited interventions/injuries for the target knee
- Missing more than 7 doses of MIV-711
- Discontinuation from the study

Note: this is not an exhaustive list of deviations, these are only the deviations specified per protocol. The discussion during the data review meeting post data base soft lock will review all deviations collected at each site and it will be decided to which analysis set each patient belongs.

6. General Considerations for Data Presentations

In this study IMP refers to any amount of the treatments defined in section 3.5, regardless of the time or period of administration.

Data for all patients enrolled in study MIV-711-202 who receives at least one dose of IMP will be presented in the data listings.

A patient who is enrolled in study MIV-711-202 but does not receive IMP will be included in those data listings for which they have data but will be excluded from all data summaries. Data summaries will only include those patients that receive IMP.

For those listings or data summaries where baseline and change from baseline measurements will be presented, unless stated otherwise, the baseline assessment to be used for calculating change from baseline will be the last valid assessment prior to first dose of 200 mg MIV-711. Note that the change from baseline will be calculated also for visits prior to the baseline visit, not only for visits succeeding the baseline visit.

Data from both studies for patients enrolled in study MIV-711-202 will be included in the data listings, tables and figures, as appropriate.

All pre- and post-dose assessments including unscheduled assessments will be included in the data listings. For unscheduled assessments collected pre-dose, the last assessment taken for a time point will be used in the data summaries (summary tables, figures, and statistical analysis); for all post-dose time points, the original assessment for any given time point will be used in the data summaries (summary tables, figures, and statistical analysis).

Descriptive statistics for observed values and derived change from baseline values will be tabulated by visit and study group. Continuous variables will be summarized by study group and visit, as appropriate, using descriptive statistics including: number of observations (n), mean (arithmetic), median, standard deviation (SD), minimum, and maximum. Frequencies and percentages will be used for summarizing discrete (categorical) data by study group and visit, as appropriate. The denominator used when calculating percentages will be the number of patients assessed at a particular combination of study group and study visit, as appropriate

Safety and efficacy data that are reported as missing will be excluded from all descriptive and non-descriptive data analysis. There will be no imputation of any data. Observations that might be considered spurious (extreme relative to the majority of the data) will not be altered or removed from any presentation of the data, including the calculation of summary statistics (means, medians, etc.), unless approved by the sponsor.

For data listings, all raw data will be reported/displayed exactly as provided. For summaries of quantitative safety data, the minimum and maximum value will be reported exactly as the raw data are reported; measures of central tendency (means, medians) will be reported to one more decimal place than the raw data; measures of variance (SD) will be reported to two more decimal places than the raw data.

Unless stated otherwise there will be no adjustment for multiple comparisons.

In all data presentations 'Treatment' will be defined as 200 mg MIV-711. Listings will include all patients and will be sorted by patient number and time point (where applicable). All derived data used in a data summary or statistical analysis will be listed.

6.1 Software

All statistical analyses will be performed using Statistical Analysis Software (SAS®) (SAS® Institute Inc., Cary, North Carolina, United States of America [USA]) Version 9.2 or higher.

7. Patient and Treatment Information

7.1 Patient Disposition

The completion status, date of completion or discontinuation, the reason for discontinuation, and the study day of withdrawal will be listed. The number of patients enrolled and the frequency and percentage of patients completing the study, patients withdrawing early, and primary reason for withdrawal will be summarized. Also included in this summary will be the numbers of patients in each of the analysis populations: ITT, PPS, SAF.

7.2 Patients Excluded from Analysis Populations

Each patient excluded from one of the analysis populations will be listed along with the reason for their exclusion.

7.3 Eligibility Criteria

All enrolled patients who did not meet an inclusion criterion and all enrolled patients who met an exclusion criterion will be listed.

7.4 Exclusion Tests

Results of the exclusion tests will be listed. These will include laboratory tests performed prior to dosing for: FSH testing, and urine drug screen.

7.5 Protocol Deviations

All reported protocol deviations will be listed.

7.6 Demographic Data

Demographic and baseline characteristics will be evaluated for Group A and Group B. Demographic information will be listed. Descriptive statistics will be obtained for the continuous variables: height, age, BMI, and body weight and presented overall. Frequencies and percentage of patients will be tabulated for the categorical variables ethnicity, race, and gender.

Patient height will be obtained from MIV-711-201 study.

7.7 Medical History

Medical and surgical history data recorded prior to dosing will be listed for each patient. Medical history will be coded using the MedDRA (Version 18.1).

Only those body systems where a condition or abnormality has been reported will be listed.

Any medical history data with start date after visit 2 in the MIV-711-201 study will be flagged in the medical history data listing. This data was collected as adverse event data during the MIV-711-201 study.

AEs from the MIV-711-201 study are recorded as medical history in the MIV-711-202 study. Any medical history data with start date after visit 2 in the MIV-711-201 study (i.e AEs) and which were ongoing at visit 1 in the MIV-711-202 study will be flagged in the medical history data listing.

Flagged medical history items will be summarized by system organ class, preferred term, and treatment.

7.8 Prior and Concomitant Medication

Prior and concomitant medications will be coded using WHO Drug (September 2015 version). These medications will be classified by Anatomical Therapeutic Chemical (ATC) categories.

Prior and Concomitant Medications will be listed by patient.

Summary tables of the number of patients and percentage of patients by group and ATC classification will be provided for prior and concomitant medications. ATC level 1 and ATC level 3 will be used.

Relevant prior and concomitant medication from MIV-711-201 will be recorded as prior medication in the MIV-711-202 study. Two indicative variables/flags will be added to the data listings/database:

1. Prior medications with start date after visit 2 in the MIV-711-201 study will be flagged in the data listing.

2. Prior medications ongoing after visit 1 in the MIV-711-202 study will be flagged in the data listing.

Flagged prior medications will be summarized by ATC level 1 and ATC level 3, and treatment group.

7.9 Dose Administration

Information collected per the dose administration CRF will be listed including patient number, visit, date and time of administration, number of capsules dispensed and number of capsules returned.

The number and percentage of patients who received IMP will be summarized for each on site visit. Descriptive statistics will be used to summarize drug accountability as the number of capsules returned for each on site study visit by treatment.

Compliance will be derived as the number of days patient were exposed to IMP. 100% compliance will be considered for dosing during the period Visit 2 to Visit 5.
The number of capsules used will be derived as the number of capsules dispensed minus the number of capsules returned. Subjects with less than 100% compliance will be identified among those who have results for "Reason not all unused Capsules returned". The compliance will not be calculated for withdrawn patients, as the date of the last IMP dose taken is not captured in the database.

8. Pharmacodynamic Analysis – Efficacy

The baseline will be the last valid assessment prior to first dose of 200 mg MIV-711, i.e. the baseline visit is defined as

- Visit 2 in study MIV-711-201 for study group A
- Visit 8 in study MIV-711-201 for study group B

The exception is for the biomarkers in study group B, where the baseline visit is defined as visit 2 in the present study (MIV-711-202).

The change from baseline for visit X will be calculated as the (visit X – baseline visit) difference in observed values. Note that the change from baseline will be calculated for all visits in study MIV-711-201 and study MIV-711-202 where the actual endpoint has

been observed, i.e. not only for visits in study MIV-711-202 succeeding the baseline visit.

All efficacy analyses will be made on the ITT population if not stated otherwise.

8.1 Imorphics MRI Assessments

The analyses of the imporphics MRI will be made on the ITT group and on the PPS population.

The observed values and the derived change from baseline values will be listed and summarized descriptively for the following MRI variables:

- MRI of the bone area of the medial femur for the target knee.
- MRI of the cartilage thickness for the target knee.
    - CM_FEMUR_THCTAB: Average thickness of cartilage in the central medial femur region
    - CM_TIBIA_THCTAB: Average thickness of cartilage in the central medial tibia region
- MRI of the total bone marrow lesion volume for the target knee

8.1.1 Statistical Analysis – Imorphics MRI Assessments

A linear mixed effects model will be used to assess the behaviour of the MRI response over the entire period of the two studies, i.e. from visit 2 in study MIV-711-201 to visit 5 in study MIV-711-202. The model will include fixed factors for study group (A or B), visit, group*visit interaction, baseline analgesic user (Yes/No), and random effect for site and patient.

Patients considered analgesic users at baseline will be identified via concomitant medication analgesic usage. A patient exposed to a prescribed analgesic and ongoing medication at time of the first 200 mg MIV-711 intake (visit 2 study MIV-711-201 for patients in group A and visit 2 study MIV-711-202 for group B) will be considered as a baseline analgesic user.

The dependent variable in the linear mixed model is the observed MRI score. Separate mixed model analyses will be considered for each of the MRI endpoints noted in section 8.1. The following SAS code will be used as default, but a reduced model may be used in case of convergence issues:

```
PROC MIXED data=;
  CLASS patient visit group baseline_conmed_pain_use;
```

```
 MODEL MRI_score = group visit group*visit baseline_conmed_pain_use/ DDFM=KR ;
 RANDOM site;
 REPEATED visit / SUBJECT=patient TYPE=UN;
 LSMEAN group*visit  / diff CL ALPHA=0.1  ;
RUN;
```

In case of convergence issues, a reduced model will be used to achieve convergence. The first two model reductions that will be considered are the following:

1. Simplify the covariance structure by using a compound symmetry covariance structure instead of unstructured.
2. Omitt the random effect of site

The mean level and the change from visit 2 in study MIV-711-201 will be estimated for each population*visit combination in the model above together with the corresponding 90% confidence interval. The estimates and confidence intervals will be tabulated and visualized over visits with the two groups in the same table/figure (see example figures and example table below). In this example table and example figures (Figure 1, Figure 2 and Table 1), ‘Population A’ and ‘Population B’ refer to Group A and Group B.

Figure 1 Example figure of estimated mean levels

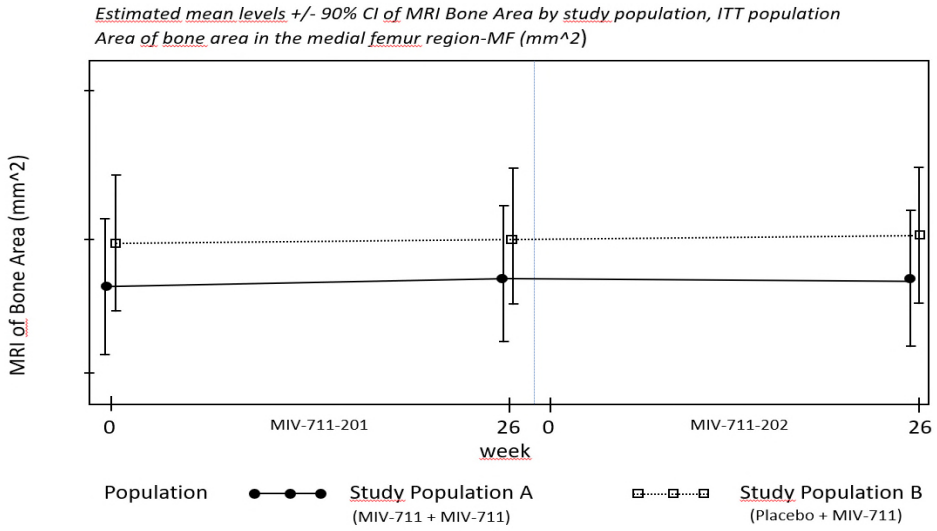


Figure 2 Example figure of estimated change from visit 2 (MIV-711-201)

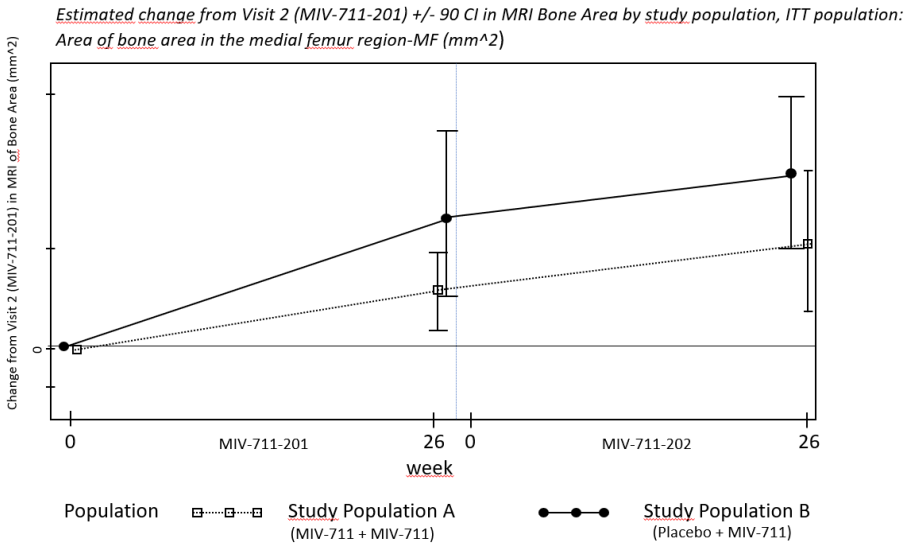


Table 1 Example table of statistical analysis corresponding to Figure 1 and Figure 2.

				Estimated Mean level		Estimated Change from Visit 2, Study MIV-711-201	
Endpoint	Population	Visit	N	LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
MRI of Bone Area	A	V2:201	nn	xx	(xx, xx)		
Medial femur region		V8:201	nn	xx	(xx, xx)	xx	(xx, xx)
		V5:202	nn	xx	(xx, xx)	xx	(xx, xx)
	B	V2:201	nn	xx	(xx, xx)		
		V8:201	nn	xx	(xx, xx)	xx	(xx, xx)
		V5:202	nn	xx	(xx, xx)	xx	(xx, xx)

8.2 MOAKS MRI Assessments

The MOAKS variables below will be listed for each patient.

MOAKS Variables

- Bone Marrow Lesions (BMLs) and cysts (15 regions)
  - Number of BML cyst
  - Size of BML
  - % that is BML
- Cartilage Assessment (14 regions)
  - Size of any Cartilage Loss: 0=’Normal’, 1=’<10% Area’, 2=’10-75% Area’, 3=’>75% Area’, 9=’Not Evaluable’
  - Percentage Full Thickness Loss: 0=’Normal’, 1=’<10% Region’, 2=’10-75% Region’, 3=’>75% Region’, 9=’Not Evaluable’
- Osteophytes (12 regions): 0=’None’, 1=’Small’, 2=’Medium’, 3=’Large’, 9=’Not Evaluable’
- Hoffa-Synovitis: 0=’None’, 1=’Mild’, 2=’Moderate’, 3=’Severe’
- Effusion-Synovitis: 0 = ‘Physiologic Amount’, 1 = ‘Small’, 2 = ‘Medium’, 3 = ‘Large’

For each patient and visit, the number of subregions/locations impacted by a MOAKS MRI feature will be calculated for the following variables:

- Number of BMLs and cysts.
- Size of any Cartilage Loss.
- Osteophytes

A subregion/location is considered to be by the MRI feature if it has score =1 or higher.

Shift tables by group will be tabulated for the shift from baseline to visit 5 for the number of subregions impacted by the MRI feature for the three MOAKS variables above.

8.3 Analysis of Patient Reported Outcomes (PROs)

8.3.1 NRS Pain Data

The observed values and the derived change from baseline values will be listed and summarized descriptively for the following NRS knee pain variables:

- Overall of pain severity in the target knee last week (SDTM: Overall pain severity in target knee
- Worst pain severity in target knee (SDTM: Worst pain severity in target knee)
- Overall pain severity in other knee (SDTM: Overall pain severity in other knee)
- Global Disease Activity (SDTM: How active was target knee arthritis)
- Satisfaction with target knee function (SDTM: How satisfied are you with target knee function)

8.3.1.1 Statistical Analysis of the NRS Pain Data

The statistical analysis of NRS Pain data will be performed using the same statistical analysis as for the Imorphics MRI described in in section 8.1.1. The output of the statistical analysis will be similar (see example figures and table section 8.1.1.) but will be based on the visits when the NRS assessments were conducted.

8.3.2 Intermittent and Constant Osteoarthritis Pain (ICOAP) Knee Version

The observed values and the derived change from baseline values will be listed for the three transformed ICOAP scores (Constant Pain, Intermittent Pain, and Total Pain). The transformed ICOAP will take values between 0 and 100 and will be calculated as follows:

Constant pain subscale

To calculate the Total constant pain subscale, sum the scores within each time point for items IP1 through IP5. Maximum constant pain score ranges from 0 to 20.
This score can be transformed to a score out of 100 using the following formula:
(Total constant pain score / 20) x 100

Intermittent pain subscale

To calculate the total intermittent pain subscale, sum the scores within each time point for items IP6 through IP11. Maximum intermittent pain subscale ranges from 0 to 24.
This score can be transformed to a score out of 100 using the following formula:
(Total intermittent pain score / 24) x 100

Total pain score
To calculate the total ICOAP score, sum the constant and intermittent pain subscales within each time point. Maximum total pain score ranges from 0 to 44.
This score can be transformed to a score out of 100 using the following formula:
(Total pain score / 44) x 100

8.3.3 **Analysis of WOMAC**

Normalized WOMAC scores, taking scores between 0 and 100, will be derived for each of the three WOMAC domains: WOMAC pain, WOMAC function, and WOMAC stiffness as follows:

For each subject and each scheduled time point derive the total WOMAC score for each of the three domains:

- Total WOMAC Pain Score (Total_WOMAC_Pain_50) = Sum of the five WOMAC pain item scores. Denote this new variable in the data set as 'WOMAC_Pain_50'.
- Total WOMAC Function Score (Total_WOMAC_Func_170) = Sum of all 17 WOMAC difficulty item scores. Denote this new variable in the data set as 'WOMAC_Func_170'
- Total WOMAC Stiffness Score (Total_WOMAC_Stiff_20) = Sum of the 2 WOMAC stiffness item scores. Denote this new variable in the data set as 'WOMAC_Stiff_20'.

Each of the total WOMAC scores will be normalized using the following multipliers:

- Normalized WOMAC PAIN Score = Total_WOMAC_Pain_50 x 2.
- Normalized WOMAC Function Score = Total_WOMAC_Func_170 ÷ 1.7.
- Normalized WOMAC stiffness Score = Total_WOMAC_Stiff_20 x 5.

8.3.3.1 Statistical analysis of WOMAC

The statistical analysis of the three normalized WOMAC scores will be performed using the same statistical analysis as for the Imorphics MRI described in section 8.1.1. An additional linear model will be included for the individual WOMAC Pain score WOMAC1-Pain - walking on a flat surface. The output from these statistical analysis will be similar to that for the imorphics and NRS data (see example figures and table section 8.1.1.), except the analysis will be based on the visits when the WOMAC assessments were conducted.

8.3.4 (OARSI)-OMERACT Responder Criteria

The OARSI-OMERACT response (Yes, No) will be derived from the PROs from the WOMAC scores (the Normalized WOMAC PAIN Score and the Normalized WOMAC Function Score as defined in section 8.3.3 and the Patient Global Assessment (NRS question 4: Over the past week, how active do you think your knee arthritis has been?).

The OARSI-OMERACT response (Yes, No) will be calcuted for visit 5 MIV-711-202 for each patient by the following steps:

Step 1. Normalize the Patient Global Assessment score so it takes values between 0 and 100 in the same way as the Normalized WOMAC PAIN Score and th Normalized WOMAC Function Score described in section 8.3.3:

a) Normalized Global Assessment Score:
NRSACT_100 = (Global Assessment Score) ☒ 10.

Step 2. Use the normalized scores to derive change from baseline and percentage change from baseline for visit 5 MIV-711-202:

Denote the change from baseline scores as:

- CHG_WOMAC_PAIN_100
- CHG_WOMAC_FUNC_100
- CHG_NRSACT_100

Denote the percentage change from baseline scores as:

- PCHG_WOMAC_PAIN_100
- PCHG_WOMAC_FUNC_100
- PCHG_NRSACT_100

Percentage change from baseline will be calculated as:
((Visit 5 Score –baseline Score) ÷ aseline Score) ☒ 100
.

Step 3. Derive Responder OARSI-OMERACT (Yes, No): In assessing for a positive OMERACT response, patient improvement (Response = Yes) is associated with decreases (negative changes) from baseline and (negative) percentage (changes) decreases from baseline. The different criteria are quantified in the tables below.

Case 1: using the change from baseline and percentage change from baseline scores for WOMAC pain and WOMAC function (from step 2), an OMERACT responder will be flagged as ‘Yes’ if either of the following 2 criteria are satisfied:

Criteria		Decrease from Baseline		Percentage Decrease from Baseline	OMERACT Responder
1	WOMAC Pain	≥ 20	and	≥ 50%	Yes
2	WOMAC Function	≥ 20	and	≥ 50%	Yes

Case 2: using the change from baseline and percentage change from baseline scores for WOMAC pain, WOMAC function, and global assessment score (from step 2), an OMERACT responder will be flagged as 'Yes' if at least 2 of the following 3 criteria are satisfied:

Criteria		Decrease from Baseline		Percentage Decrease from Baseline	OMERACT Responder
3	WOMAC Pain	≥ 10	and	≥ 20%	Yes
4	WOMAC Function	≥ 10	and	≥ 20%	Yes
5	Global Assessment NRS	≥ 10	and	≥ 20%	Yes

A subject is a 'Yes' responder if either of criteria 1 or 2 are satisfied. If neither criteria 1 or 2 are satisfied, criteria 3, 4 and 5 will be checked.

A listing will be created that presents each patient's responder status by visit. Included in this listing will be the associated change from baseline and percent change from baseline values.

8.3.5 **Global Improvements**

Global improvements in knee problem, knee pain and knee function that were recorded on a 6-point Likert scale: completely better, much better, better, no change, worse, much worse. All data will be listed for each patient.

8.3.6 **Quality of Life PRO – EQ-5D-5L**

The observed values and the derived change from baseline values for the six items of Quality of Life PRO – EQ-5D-5L described in section 4.5.3.6 will be listed and summarized descriptively.

8.3.7 E-diary for Patient Pain

All data collected in e-diary fomat will be listed for each patient.

The observed values and the change from baseline values for the derived e-diary summary scores described in section 8.3.7.1 below will be listed and summarized descriptively.

8.3.7.1 Derived e-diary variables

Three e-diary variables will be derived:

- NRS score
- Percentage score for analgesic usage last 12 hours
- Severity and extent of their pain medication usage

For each e-diary endpoint and visit, a patient's summary value will be calculated by using the e-diary assessments recorded at the study days asscociated with that study visit. The study days asscociated with study Visit 'x' will be identified as follows: beginning at the last date of assessment associated with Visit 'x' and including up to 14 days prior to the visit recorded within 19 calendar days prior to the date of Visit 'x'. If there are less than 10 days of recorded e-diary assessment within those 19 calendar days, the summary value will not be calculated for that visit.

NRS score

The derived summary scores for e-diary NRS scores associated with each visit will be obtained as the arithmetic mean (the average) of all e-diary NRS scores observed during the study days associated with that visit (as defined above). Separate e-diary NRS summary scores will be provided for AM and PM response. In addition, the overall 24 hour summary score will be calculated as the mean of the AM and PM summary scores for each visit. The overall 24 hour summary score will only be calculated if both mean AM and mean PM scores are available.

Percentage score for analgesic usage last 12 hours

Each patient's 'pain medication usage over the last 12 hours (Yes/No)' will be calculated as the percentages of days with a YES-response of the study days associated with that visit (as defined above). This will provide each patient with a percentage score for analgesic use for each study visit and for each of AM, PM. The denominator for AM and PM percentage calculations will be the actual number of days assessed, such that the number of days is at least 10 days and less than or equal to 14 days. The overall percentage, combining AM and PM measures, will be calculated as the mean of the AM and PM percentages:

- Overall percentage = (xx/AM denominator + yy/PM denominator)/2

where 'xx' is the count of AM 'Yes' responses, 'yy' is the count of PM 'Yes' responses.

Severity and extent of their pain medication usage

Each patient's summary score for severity and extent of their pain medication usage ('More than Normal', 'Normal', 'Less than normal') will be the worst (most severe) response recorded during the study days associated with each visit (as defined above). The summary score will only be calculated if the patient responded 'YES' to 'Pain medication Usage' within the study days associated with the actual visit (as defined above). Summaries will be provided by visit, with separate summary score for AM and PM. The overall 24 hour summary score will be the worst (most severe) of the AM and the PM summary score and will be calculated if the AM and the PM summary score are available.

8.3.7.2 Statistical analysis of e-diary scores

The derived e-diary NRS score will be analysed using the same statistical analysis as for the Imorphics MRI described in detail in section 8.1.1. Outputs from these statistical analysis will be similar to that as presented for the MRI data (see example figures and table section 8.1.1.) however outputs and analysis of the e-diary scores will be based on the visits when the e-diary assessments were recorded.

8.3.8 Biomarkers from Serum and Urine Samples

The observed values and the change from baseline values for the serum CTX-I and urinary CTX-II biomarkers will be listed and summarized descriptively. Note the baseline visit is defined as visit 2 in study MIV-711-202 for study Group B.

Time-Integrated-Concentrations (TIC) will be derived for each serum CTX-I and urinary CTX-II biomarkers. For each biomarker the mean TIC value and the standard deviation (SD) of the TIC regarding the time period on drug will be derived. Thus, for group A the time period will include 26 + 26 weeks whereas the time period for group B will be the 26 weeks in study MIV-711-202. For each biomarker a Z-score will be derived by subtracting the mean and dividing by SD. TIC results and associated Z-scores will be listed and summarized for each subject.

Box plots will be used to visualize the distribution of TIC response and biomarker Z-score.

8.3.8.1 Statistical analysis biomarkers from serum and urine samples

The statistical analysis of the serum CTX-I and urinary CTX-II biomarkers will be performed using the same statistical analysis as for the Imorphics MRI described in in section 8.1.1. Outputs from these statistical analysis will be similar to that as presented for the MRI data (see example figures and table section 8.1.1.) however outputs and analysis of the biomarker scores will be based on the visits when the biomarker assessments were recorded.

8.3.9 Brief Medication Questionnaire

Brief medication questionnaire results will be summarized for the number and percentage of patients reporting:

- each medication taken
- each indication
- combination of medication taken per indication
- compliance for each medication taken

Descriptive summary tables will be presented separately for Group A and Group B. Summary tables and listings for brief medication questionnaire will only be based on data from MIV-711-202 study.

9. Safety Analysis

For the safety outcomes, for study Group A, changes from baseline will be assessed using the Visit 2 baseline data from MIV-711-201. For study Group B, changes from baseline will be assessed using the Visit 2 data from Study MIV-711-202.

The change from baseline for visit X will be calculated as the (visit X – baseline visit)-difference in observed values. Note that the change from baseline will be calculated for all visits in study MIV-711-201 and study MIV-711-202 where the actual endpoint has been observed, i.e. not only for visits in study MIV-711-202 succeeding the baseline visit.

All safety summary tables will be based on the SAF population.

Descriptive summaries for safety will be presented by study group and visit, as appropriate.

9.1 Adverse Events

All AEs reported will be coded and classified according to MedDRA version 18.1.
A treatment-emergent AE (TEAE) will be defined as an AE that begins or that worsens in severity after IMP has been administered.

Non-treatment emergent adverse events (NTEAE): AEs that occurred before the administration of IMP and did not worsen in severity or relationship after exposure to IMP.

All AE data as captured on the CRF for MIV-711-202 study will be listed by patient. All AEs from MIV-711-201 study for those patients admitted into the MIV-711-202 study will also be listed. All serious AEs (SAEs) will be listed. A listing of all AEs leading to treatment discontinuation will be presented.

Unless specified otherwise, all adverse event summaries will include the TEAEs only and adverse event summary counts of AEs will be the number of patients reporting adverse events and not the number of events reported. The number and percentage of patients with adverse events will be tabulated by body system (SOC) and preferred term (PT) for each group (A, B) and study (MIV-711-201, MIV-711-202). A patient with multiple adverse events within a body system is only counted once towards the total of that body system. If the same AE (preferred term) is reported several times for the same patient, it will only appear once for that specified treatment in the summary tables.

For patients with multiple adverse events of the same preferred term and of different severities, the AE with the highest assessment of severity will be used in the summaries presented by severity.

A general summary of all treatment-emergent adverse events will show the number and percentage of patients, as well as the number of events, according to the following categories:

- All treatment emergent adverse events
- 'Related' treatment emergent adverse events
- Mild treatment emergent adverse events
- Moderate treatment emergent adverse events
- Severe treatment emergent adverse events
- Serious treatment emergent adverse events
- Treatment emergent adverse events leading to early termination
- Deaths

Other summary tables for adverse events will include:

- Number and Percentage of Patients with Treatment Emergent Adverse Events by System Organ Class, and Preferred Term
- Number and Percentage of Patients with Treatment Emergent Adverse Events 'Related to IMP' by System Organ Class, Preferred Term, and Severity.
- Number and Percentage of Patients with Serious Treatment Emergent Adverse Events by System Organ Class, and Preferred Term
- Number and Percentage of Patients with Treatment Emergent Adverse Events Leading to Discontinuation by System Organ Class, and Preferred Term
- Number and Percentage of Patients with Treatment Emergent Adverse Events by Preferred Term per Frequency of Occurrence

All AE summary tables will display the AEs that occurred in both MIV-711-201 and MIV-711-202 studies for patients that were dosed in MIV-711-202. For tabulations of AEs by study group, any AE that starts on or after administration of the first dose received in MIV-711-201 and before the first dose received in MIV-711-202, will be assigned to the the 201 study group. Any AE occurring after the first dose administered in MIV-711-202 will be assigned to the 202 study group.

If a subject has multiple AEs with the same preferred term but occurring after each dose administration (MIV-711-201 and MIV-711-202), then one AE will be counted for each treatment administration. Adverse events that emerge in the first treatment period (201) and carry over into the next period (202) will be attributed to only the period in which the AE emerged (201). Such AEs that carry over into MIV-711-202 will be recorded as part of MIV-711-202 medical history.

9.2 Clinical Safety Laboratory Tests (Hematology, Chemistry, Urinalysis)

9.2.1 Hematology and Chemistry

A by-patient listing of all observed chemistry and hematology laboratory data will be provided. Laboratory results outside the normal range will be flagged. The abnormal values will be flagged with 'L' (low) for values below the lower limit of the laboratory's normal range or 'H' (high) for values above the upper limit of the laboratory's normal range. Abnormal values will be graded as not clinically significant (NCS) or clinically significant (CS). Clinically significant laboratory results will be included in the AE listings.

The observed values of all safety laboratory assessments for clinical chemistry and hematology will be summarized using descriptive statistics showing the number of

observations (n), mean, median, SD, minimum, and maximum value. Table summaries will be presented by time point.

Baseline values for all clinical chemistry and hematology parameters will be categorized as being below the normal range (Low), within the normal range (Normal), and above the normal range (High). In addition, the minimum and maximum score over visits post baseline will be calculated and categorized into Low, Normal and High. Note that the minimum/maximum are taken over visits post the baseline visit, i.e. visits when the patients are on 200 mg MIV-711. Shift from baseline tables of the minimum category score and the maximum category score will be tabulated displaying frequency counts and percentage of patients in each (low, normal, high)-matrix by study group.

All hematology, chemistry, and coagulation, laboratory parameters noted in Section 4.4.2 of this SAP will be tabulated.

9.2.2 Urinalysis

Urinalysis test results will be listed. All positive findings in the microscopic examination will be listed.

Observations outside the normal range will be flagged. The abnormal quantitative values will be flagged with 'L' for values below the lower limit of the laboratory's normal range, 'H' for values above the upper limit of the laboratory's normal range, or 'Ab' for abnormal qualitative test results. All original and unscheduled assessments will be listed.

9.3 Vital Signs

The observed data for blood pressure (systolic and diastolic), heart rate (pulse), pulse oximetry, and body temperature will be listed by patient, and time point. Change from baseline values for blood pressure (systolic and diastolic), and heart rate (pulse) will be derived and listed. The overall qualitative assessment for vital signs will be listed.

For systolic and diastolic blood pressure and heart rate, the observed values and change from baseline data will be summarized by group and time point. Table summaries will include descriptive statistics showing the number of observations (n), mean, SD, median, minimum, and maximum value.

Figures of the observed mean response will be used to visualize blood pressure and heart rate response by time point. The two study groups will be shown in the same figure.

9.4 12-Lead Safety ECG

Observed quantitative results for RR, PR, QRS, QT, QTcB (corrected QT according to Bazett), QTcF (corrected QT according to Fridericia) and heart rate will be listed for each patient. Change from baseline for QT, QTcB, QTcF will be derived and listed.

The overall qualitative ECG assessment Abnormal NCS, Abnormal CS, and any comments will be listed for each patient.

For QT, QTcB, QTcF the observed and change from baseline data will be summarized by study group and time point. Summaries will include tables of descriptive statistics showing the number of observations (n), mean, SD, median, minimum, and maximum value.

Figures of the observed mean response will be used to visualize QTcB and QTcF response by time point. The two stdy groups will be shown in the same figure.

The number and percentage of patients having observed QT, QTcB, QTcF values that satisfy the following conditions will be summarized by time point and and study group:

- ≤ 450 msec
- $450 <$ to ≤ 480 msec
- $480 <$ to ≤ 500 msec
- > 500 msec

The number and percentage of patients having change from baseline QT, QTcB, QTcF values that satisfy the following conditions will be presented by time point and study group:

- ≤ 0 msec
- > 0 to ≤ 30 msec
- > 30 to ≤ 60 msec
- > 60 msec

9.5 Physical Examination and Weight

All abnormal physical exam findings (pre and post-dose assessments) will be listed.

Patient weight will be collected and listed. Patient weight data wil be obtained from the MIV-711-201 study as weight was not collected in MIV-711-202.

9.6 Phone Call to Assess Safety

Results of this assessment will be listed for each patient and each visit.

10. Reporting Output

The following details the requirements and specifications for the presentation of the tables, figures and listings (TFLs) as set out in the TFL shells.

The tables, listings, figures and any non-descriptive statistical analysis will be produced using Unix SAS® Software (Version 9.2 or higher). The REPORT procedure will be used to produce all tables and listings; SAS/GRAPH will be used to produce all figures.

Tables, listings, and figures will be produced in the order that they appear in the textual sections of the plan.

All tables, listings, and graphs will be produced to landscape orientation using Courier New 8pt font and will be incorporated into a MS Word document as a (RTF) rich text file (margins: top, left, right, and bottom: 1 inch). Details are provided below.

- A separate RTF document will be created for each table, figure and listing individually.
- All TFLs will be produced in a landscape format, as far as is feasible.
- The standard font size and font type are "8 point", "Courier New" for all TFLs.
- Every page of each output will contain a footer indicating the date and time when the output was produced.
- Page numbering of tables and listings will use the format "Page X of Y". Page numbering for figures will be consecutive integers.
- The ordering of visits will be chronological
- Footnotes are left justified.

11. Summary Tables

TLF Number	Title
Table 14.1.1	Patient Disposition – All Enrolled Patients
Table 14.1.2	Demographics - Continuous Variables, ITT Population
Table 14.1.3	Demographics - Categorical Variables, ITT Population
Table 14.1.4	Prior Medications, ITT Population
Table 14.1.5	Concomitant Medications, ITT Population
Table 14.1.6	Flagged Prior Medications, ITT Population
Table 14.1.7	Flagged Medical History, ITT Population
Table 14.1.8	Dose Administration - Number and Percentage of Patients Who Received IMP by Visit, PPS Population
Table 14.1.9	Dose Administration – Summary of Drug Compliance, PPS Population
Pharmacodynamics	
Table 14.2.1.1	Imaging variables - MRI of Bone Area for the Target Knee Observed and Change from Baseline Summary, ITT Population
Table 14.2.1.2	Imaging variables - MRI of Cartilage Thickness for the Target Knee Observed and Change from Baseline Summary, ITT Population
Table 14.2.1.3	Imaging variables - MRI of Total BML Volume for the Target Knee Observed and Change from Baseline Summary, ITT Population
Table 14.2.1.4	Imaging variables - MRI of Bone Area for the Target Knee Observed and Change from Baseline Summary, PPS Population
Table 14.2.1.5	Imaging variables - MRI of Cartilage Thickness for the Target Knee Observed and Change from Baseline Summary, PPS Population
Table 14.2.1.6	Imaging variables - MRI of Total BML Volume for the Target Knee Observed and Change from Baseline Summary, PPS Population
Table 14.2.1.7	Statistical Analysis – MRI of Bone Area for the Target Knee in Patients with Moderate Osteoarthritis, ITT Population
Table 14.2.1.8	Statistical Analysis - MRI of Cartilage Thickness for the Target Knee in Patients with Moderate Osteoarthritis, ITT Population
Table 14.2.1.9	Statistical Analysis - MRI of Total BML Volume for the Target Knee in Patients with Moderate Osteoarthritis, ITT Population
Table 14.2.2.1	Imaging variables - MOAKS Bone Marrow Lesion (BML) and Cyst Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population
Table 14.2.2.2	Imaging variables - MOAKS Cartilage Assessments Size of any Cartilage Loss Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population
Table 14.2.2.3	Imaging variables - MOAKS Cartilage Assessments Percentage of Full Thickness Loss Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population
Table 14.2.2.4	Imaging variables - MOAKS Osteophyte Size Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population

Table 14.2.3.1	NRS Scores Observed and Change from Baseline Summary, ITT Population
Table 14.2.3.2	Statistical Analysis of NRS Scores, ITT Population
Table 14.2.4.1	Normalized WOMAC Scores Observed and Change from Baseline Summary - ITT Population
Table 14.2.4.2	Individual WOMAC Scores Observed and Change from Baseline Summary, ITT Population
Table 14.2.4.3	Statistical Analysis – Normalized WOMAC Scores, ITT Population
Table 14.2.4.4	Statistical Analysis – WOMAC Pain Score (walking on a flat surface), ITT Population
Table 14.2.5	EQ-5D-5L Health Rating Score Response Observed and Change from Baseline Summary, ITT Population
Table 14.2.6.1	E-Diary NRS Scores Observed and Change from Baseline Summary, ITT Population
Table 14.2.6.2	Statistical Analysis of e-diary NRS Assessment, ITT Population
Table 14.2.6.3	E-Diary Observed and Change from Baseline Summary of the Percentage of 'Yes' Scores for Analgesic Useage, ITT Population
Table 14.2.6.4	E-Diary Pain Medication Usage Over Last 12 Hours Number and Percentage of Patients with each Reported Severity Category, ITT Population
Table 14.2.7.1	Efficacy Biomarkers from Serum and Urine Samples - Summary of Observed and Change from Baseline Values, ITT Population
Table 14.2.7.2	Time-Integrated Concentrations (TIC) and Their Z-scores for Efficacy Biomarkers from Serum and Urine Samples Summary of Observed Values ITT Population
Table 14.2.7.3	Statistical Analysis – Efficacy Biomarkers from Serum CIX-I and Urine CIX-II Samples, ITT Population
Table 14.2.8.1	Brief Medication Questionnaire - Number and Percentage of Patients with each Medication Used by Visit and Group, ITT Population
Table 14.2.8.2	Brief Medication Questionnaire - Number and Percentage of Patients with each Indication by Visit and Group, ITT Population
Table 14.2.8.3	Brief Medication Questionnaire - Number and Percentage of Patients with each Medication by Indication, Visit and Group, ITT Population
Table 14.2.8.4	Brief Medication Questionnaire Compliance - Number and Percentage of Patients Who Missed Taking their Medication by Visit, ITT Population
Safety	
Table 14.3.1.1	Summary of Treatment Emergent Adverse Events , SAF Population
Table 14.3.1.2	Number and Percentage of Patients with Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Group, SAF Population
Table 14.3.1.3	Number and Percentage of Patients with Treatment Emergent Adverse Events 'Related to IMP' by System Organ Class, Preferred Term, Severity, and Group, SAF Population
Table 14.3.1.4	Number and Percentage of Patients with Serious Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Group, SAF Population
Table 14.3.1.5	Number and Percentage of Patients with Treatment Emergent Adverse Events Leading to Discontinuation by System Organ Class, Preferred Term, and Group, SAF Population

Table 14.3.1.6	Number and Percentage of Patients with Treatment Emergent Adverse Events by Frequency, Preferred Term, and Group
Table 14.3.2.1	Clinical Laboratory Chemistry Summary of Observed Values, SAF Population
Table 14.3.2.2	Clinical Laboratory Hematology Summary of Observed Values, SAF Population
Table 14.3.2.3	Clinical Laboratory Chemistry – Shift From Baseline to Maximum Value, SAF Population
Table 14.3.2.4	Clinical Laboratory Chemistry – Shift From Baseline to Minimum Value, SAF Population
Table 14.3.2.5	Clinical Laboratory Hematology – Shift From Baseline to Maximum Value, SAF Population
Table 14.3.2.6	Clinical Laboratory Hematology – Shift From Baseline to Minimum Value, SAF Population
Table 14.3.3	Vital Signs Blood Pressure and Heart Rate Summary of Observed and Change from Baseline Values, SAF Population
Table 14.3.4.1	12 Lead ECG – Summary of Observed and Change from Baseline Values SAF Population
Table 14.3.4.2	12-Lead ECG – Categorical Summary of Observed Values, SAF Population
Table 14.3.4.3	12-Lead ECG – Categorical Summary of Change From Baseline, SAF Population

12. Figures

TLF Number	Title
Figure 14.2.1.1	Estimated Mean ± 95% CI for MRI of Bone Area by Week and Group, ITT Population
Figure 14.2.1.2	Estimated Mean ± 95% CI for MRI of Cartilage Thickness by Week and Group, ITT Population
Figure 14.2.1.3	Estimated Mean ± 95% CI for MRI of Total BML Volume by Week and Group, ITT Population
Figure 14.2.1.4	Estimated change from Visit 2 MIV-711-201 ± 95% for MRI of Bone Area by Week and Group, ITT Population
Figure 14.2.1.5	Estimated change from Visit 2 MIV-711-201 ± 95% for Cartilage Thickness by by Week and Group, ITT Population
Figure 14.2.1.6	Estimated change from Visit 2 MIV-711-201 ± 95% for MRI of Total BML Volume by Week and Group, ITT Population
Figure 14.2.1.7	Estimated change from Visit 2 MIV-711-201 ± 95% for MRI of Bone Area by Week and Group, PPS Population
Figure 14.2.1.8	Estimated change from Visit 2 MIV-711-201 ± 95% for Cartilage Thickness by Week and Group, PPS Population
Figure 14.2.1.9	Estimated change from Visit 2 MIV-711-201 ± 95% for MRI of Total BML Volume by Week and Group, PPS Population
Figure 14.2.3.1	Estimated Mean ± 95% CI for NRS Items by Week and Group, ITT Population
Figure 14.2.3.2	Estimated change from visit 2 MIV-711-201 ± 95% CI for NRS Items by Week and Group, ITT Population
Figure 14.2.4.1	Estimated Mean ± 95% CI for WOMAC Items by Week and Group, ITT Population
Figure 14.2.4.2	Estimated change from visit 2 MIV-711-201 ± 95% CI for WOMAC Items by Week and Group, ITT Population
Figure 14.2.4.3	Estimated Mean ± 95% CI for Normalized WOMAC Scores by Week and Group, ITT Population
Figure 14.2.4.4	Estimated change from visit 2 MIV-711-201 ± 95% CI for Normalized WOMAC Scores by Week and Group, ITT Population
Figure 14.2.5.1	Estimated Mean ± 95% CI for NRS E-Diary by Week and Group, ITT Population
Figure 14.2.5.2	Estimated change from visit 2 MIV-711-201 ± 95% CI for NRS e-diary by Week and Group, ITT Population
Figure 14.2.5.3	Estimated Mean ± 95% CI for Percentage Score E-Diary Analgesic Usage by Week and Group, ITT Population
Figure 14.2.5.4	Estimated change from visit 2 MIV-711-201 ± 95% CI for Percentage Scores of E-Diary Analgesic Usage by Week and Group, ITT Population
Figure 14.2.6.1	Estimated Mean ± 95% CI for Efficacy Biomarkers by Week and Group, ITT Population
Figure 14.2.6.2	Box Plots of Time Integrated Concentrations and their Z-Scores for Efficacy Biomarkers from Serum and Urine Samples by Group, ITT Population

Figure 14.2.7.1	Mean ± 95% CI Profiles of Observed Systolic Blood Pressure by Week and Group, SAF Population
Figure 14.2.7.2	Mean ± 95% CI Profiles of Observed Heart Rate by Week and Group, SAF Population
Figure 14.2.8.1	Mean (95% CI) Profiles of Observed QTcB Interval by Week and Group, SAF Population
Figure 14.2.8.2	Mean (95% CI) Profiles of Observed QTcF Interval by Week and Group, SAF Population

13. Listings

TLF Number	Title
Listing 16.2.1.1	Patient Disposition
Listing 16.2.1.2	Patients Excluded from Analysis Populations
Listing 16.2.1.3	Enrolled Patients Who Did Not Meet All Eligibility Criteria
Listing 16.2.1.4	Exclusion Tests
Listing 16.2.2.1	Protocol Deviations
Listing 16.2.4.1	Demographics
Listing 16.2.4.2	Medical History
Listing 16.2.5.1	Prior and Concomitant Medications
Listing 16.2.5.2	Dose Administration at Clinic Visits
Listing 16.2.5.3	Dose Administration Compliance, ITT Population
Listing 16.2.5.4	Dose Administration Overall Compliance at Visit 5, ITT Population
Listing 16.2.6.1	Numerical Rating Scale of Knee Pain
Listing 16.2.6.2	Numerical Rating Scale of Knee Pain Change From Baseline
Listing 16.2.6.3	Imaging Results Imorphics - MRI of Bone Area for the Target Knee, Observed and Change from Baseline
Listing 16.2.6.4	Imaging Results Imorphics - MRI of Cartilage Thickness for the Target Knee, Observed and Change from Baseline
Listing 16.2.6.5	Imaging Results Imorphics – Total BML Volume Observed and Change from Baseline
Listing 16.2.6.7.1	Other Imaging variables - Imorphics Bone Area
Listing 16.2.6.7.2	Other Imaging variables - Imorphics Bone 3D Shape
Listing 16.2.6.7.3	Other Imaging variables - Imorphics Cartilage Thickness
Listing 16.2.6.7.4	Other Imaging variables - Imorphics Cartilage Denudation
Listing 16.2.6.7.5	Other Imaging variables - Imorphics Cartilage Reference Bone Area
Listing 16.2.6.7.6	Other Imaging variables - Imorphics BML volume
Listing 16.2.6.7.7	Other Imaging variables - Imorphics Combined
Listing 16.2.6.8.1	Other Imaging variables - MOAKS Bone Marrow Lesion (BML) and Cyst
Listing 16.2.6.8.2	Other Imaging variables - MOAKS Cartilage Assessments
Listing 16.2.6.8.3	Other Imaging variables - MOAKS Hoffa-Synovitis/Effusion-Synovitis
Listing 16.2.6.8.4	Other Imaging variables - MOAKS Ligament Assessments
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Listing 16.2.8.12	Phone Call to Assess Safety

14. Table Shells

Table 14.1.1
Patient Disposition
All Enrolled Patients

	Group A N = x	Group B N = x
Number Patients Enrolled	nn (nn.n%)	nn (nn.n%)
Completed Study	nn (nn.n%)	nn (nn.n%)
Discontinued from Study	nn (nn.n%)	nn (nn.n%)
Number Patients in ITT	nn (nn.n%)	nn (nn.n%)
Number Patients in PPS	nn (nn.n%)	nn (nn.n%)
Number Patients in SAF	nn (nn.n%)	nn (nn.n%)
Reason for Discontinuation		
Adverse Event	nn (nn.n%)	nn (nn.n%)
Protocol Deviation	nn (nn.n%)	nn (nn.n%)
Consent Withdrawn	nn (nn.n%)	nn (nn.n%)
Lost to Follow-Up	nn (nn.n%)	nn (nn.n%)
Death	nn (nn.n%)	nn (nn.n%)
Other	nn (nn.n%)	nn (nn.n%)

Table 14.1.2
Demographics – Continuous Variables
ITT Population

	Statistic	Group A N = x	Group B N = x
Age (years)	n	nn	nn
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx
Height (cm)	n	nn	nn
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx
Weight (kg)	n	nn	nn
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx
BMI (kg/m^2)	n	nn	nn
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx

Protocol Number: MIV-711-202

Table 14.1.3
Demographics – Categorical Variables
ITT Population

	Group A N = x	Group B N = x
Ethnicity		
Hispanic/Latino	nn (nn.n%)	nn (nn.n%)
Non-Hispanic/Latino	nn (nn.n%)	nn (nn.n%)
Race		
White	nn (nn.n%)	nn (nn.n%)
American Indian/Alaska Native	nn (nn.n%)	nn (nn.n%)
Asian	nn (nn.n%)	nn (nn.n%)
Native Hawaiian or other Pacific Islander	nn (nn.n%)	nn (nn.n%)
Black/African American	nn (nn.n%)	nn (nn.n%)
Other	nn (nn.n%)	nn (nn.n%)
Gender		
Female	nn (nn.n%)	nn (nn.n%)
Male	nn (nn.n%)	nn (nn.n%)

Table 14.1.4
Prior Medications
ITT Population

ATC Level 1 ACT Level 3	Group A N = x	Group B N = x
	nn (nn.n%)	nn (nn.n%)
	nn (nn.n%)	nn (nn.n%)

Table 14.1.5
Concomitant Medications
ITT Population

ATC Level 1 ACT Level 3	Group A N = x	Group B N = x
	nn (nn.n%)	nn (nn.n%)
	nn (nn.n%)	nn (nn.n%)

Table 14.1.6
Flagged Prior Medications
ITT Population

Prior Medications starting after Visit 2 in MIV-711-201

ATC Level 1 ACT Level 3	Group A N = x	Group B N = x
	nn (nn.n%)	nn (nn.n%)
	nn (nn.n%)	nn (nn.n%)

Programming note: table will be expanded to include flagging for: Prior Medications ongoing after Visit 1 in MIV-711-202

Table 14.1.7
Flagged Medical History
ITT Population

AEs ongoing during the rollover from MIV-711-201

System Organ Class Preferred Term	Group A N = x	Group B N = x
	nn (nn.n%)	nn (nn.n%)
	nn (nn.n%)	nn (nn.n%)

Table 14.1.8
Dose Administration - Number and Percentage of Patients Who Received IMP by Visit
PPS Population

Visit	Group A N = x	Group B N = x
VISIT 2 BASELINE DAY 1	nn (nn.n%)	nn (nn.n%)
VISIT 4 WEEK 14	nn (nn.n%)	nn (nn.n%)
Etc…		

Summary table will include dose administration data only for MIV-711-202 assessment times.

Table 14.1.9
Dose Administration - Summary of Drug Compliance
PPS Population

		Group A N = x	Group B N = x
	Statistic		
Total Planned Number of Days IMP exposure	n	nn	nn
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx
Total Actual Number of Capsules used	n	nn	nn
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx
Overall IMP Compliance (%)	n	nn	nn
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx

Withdrawn patients are not included in the summary
Summary table will include dose administration data only for MIV-711-202 assessment times.

Table 14.2.1.1
Imaging variables - MRI of Bone Area for the Target Knee Observed and Change from Baseline Summary
ITT Population

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
Visit 2 MIV-711-201	n	nn		nn	nn
	Mean	xx.x		xx.x	xx.x
	SD	xx.xx		xx.xx	xx.xx
	Median	xx.x		xx.x	xx.x
	Min	xx		xx	xx
	Max	xx		xx	xx
Visit 8 MIV-711-201	n	nn	nn	nn	
	Mean	xx.x	xx.x	xx.x	
	SD	xx.xx	xx.xx	xx.xx	
	Median	xx.x	xx.x	xx.x	
	Min	xx	xx	xx	
	Max	xx	xx	xx	
Visit 5 MIV-711-202	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

Programming note: source data obtained from MF_TAB: Area of bone in the medial femur region, MF

Similar table will be provided for PPS population:

Table 14.2.1.4 Imaging variables - MRI of Bone Area for the Target Knee Observed and Change from Baseline Summary, PPS Population

Table 14.2.1.2
Imaging variables – MRI of Cartilage Thickness for the Target Knee Observed and Change from Baseline Summary
ITT Population

Parameter = *Femur Region*

Visit	Statistic	Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
		N = x	N = x	N = x	N = x
Visit 2 MIV-711-201	n	nn		nn	nn
	Mean	xx.x		xx.x	xx.x
	SD	xx.xx		xx.xx	xx.xx
	Median	xx.x		xx.x	xx.x
	Min	xx		xx	xx
	Max	xx		xx	xx
Visit 8 MIV-711-201	n	nn	nn	nn	
	Mean	xx.x	xx.x	xx.x	
	SD	xx.xx	xx.xx	xx.xx	
	Median	xx.x	xx.x	xx.x	
	Min	xx	xx	xx	
	Max	xx	xx	xx	
Visit 5 MIV-711-202	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

Programming note: source data obtained from:

- CM_FEMUR_THCTAB: Average thickness of cartilage in the central medial femur region
- CM_TIBIA_THCTAB: Average thickness of cartilage in the central medial tibia region

Similar table will be created for PPS population:
Table 14.2.1.5 Imaging variables – MRI of Cartilage Thickness for the Target Knee Observed and Change from Baseline Summary
PPS Population

Table 14.2.1.3
Imaging variables – MRI of Total BML Volume for the Target Knee Observed and Change from Baseline Summary
ITT Population

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
Visit 2 MIV-711-201	n	nn		nn	nn
	Mean	xx.x		xx.x	xx.x
	SD	xx.xx		xx.xx	xx.xx
	Median	xx.x		xx.x	xx.x
	Min	xx		xx	xx
	Max	xx		xx	xx
Visit 8 MIV-711-201	n	nn	nn	nn	
	Mean	xx.x	xx.x	xx.x	
	SD	xx.xx	xx.xx	xx.xx	
	Median	xx.x	xx.x	xx.x	
	Min	xx	xx	xx	
	Max	xx	xx	xx	
Visit 5 MIV-711-202	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

Programming note: source data obtained from: TOTAL_BML_VOLUME

Similar table will be created for PPS population:
Table 14.2.1.6 Imaging variables – MRI of Total BML Volume for the Target Knee Observed and Change from Baseline Summary
PPS Population

Table 14.2.1.7
Statistical Analysis – MRI of Bone Area for the Target Knee in Patients with Moderate Osteoarthritis
ITT Population

				Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
Endpoint	Group	Week	N	LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
xxxxx	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		26 (V8: 201)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		26 (V8: 201)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Programming note: source data obtained from MF_TAB: Area of bone in the medial femur region, MF

Table 14.2.1.8
Statistical Analysis - MRI of Cartilage Thickness for the Target Knee in Patients with Moderate Osteoarthritis
ITT Population

Parameter = Average thickness of cartilage in the central medial femur region

				Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
Endpoint	Group	Week	N	LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
xxxxx	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		26 (V8: 201)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		26 (V8: 201)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Programming note: source data obtained from:

- CM_FEMUR_THCTAB: Average thickness of cartilage in the central medial femur region
- CM_TIBIA_THCTAB: Average thickness of cartilage in the central medial tibia region

Table will include results for both femur region and tibia region

Table 14.2.1.9
Statistical Analysis - MRI of Total BML Volume for the Target Knee in Patients with Moderate Osteoarthritis
ITT Population

				Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
Endpoint	Group	Week	N	LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
xxxxx	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		26 (V8: 201)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		26 (V8: 201)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Programming note: source data obtained from: TOTAL_BML_VOLUME

Table 14.2.2.1
Imaging variables - MOAKS Bone Marrow Lesion (BML) and Cyst
Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population

MOAKS Test/Examination Name = Number of BMLs

Group	Number of subregions affected	Baseline 0	1	2	3	4	5+
A N = x	0	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	4	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	5+	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
B N = x	0	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	4	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	5+	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

[1] for each examination test, the summary will consider all possible subregions associated with BML and Cyst. Maximum number of subregions is 15. In this analysis a subregion is said to be affected by a BML if the MRI score > 0. A subregion is not affected by any BML if that subregion is scored as 0.

Programming note: table will include summaries for each MOAKS test: Number of BMLs, Size of BML, % that is BML.
Follow-up data will be excluded from all MOAKs table summaries.

Table 14.2.2.2
Imaging variables - MOAKS Cartilage Assessments Size of any cartilage loss
Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population

		Baseline								
Group	Number of subregions affected [1]	0	1	2	3	4	5	6	7	8+
A N = x	0	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	4	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	5	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	6	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	7	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	8+	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
B N = x	0	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	4	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	5	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	6	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	7	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	8+	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

[1] for each examination test, the summary will consider all possible subregions associated with Cartilage Assessment. Maximum number of subregions is 14. In this analysis a subregion is said to be affected by cartilage if the MRI score > 0. A subregion is not affected by cartilage if that subregion is scored as 0.

Programming note: Similar table will be created:
Table 14.2.2.3 Imaging variables - MOAKS Cartilage Assessments Percentage of Full Thickness Loss Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population

Table 14.2.2.4
Imaging variables - MOAKS Osteophyte Size
Shift from Baseline to Visit 5 Number of Subregions Impacted by MRI Feature, ITT Population

		Baseline									
Group	Number of subregions affected [1]	0	1-3	4-5	6	7	8	9	10	11	12
A	0	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	1-3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	4-5	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	6	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	7	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	8	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	9	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	10	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	11	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	12	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
B	0	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	1-3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	4-5	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	6	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	7	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	8	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	9	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	10	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	11	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	12	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

[1] the summary will consider all possible subregions associated with osteophyte assessment. Maximum number of subregions is 12. In this analysis a subregion is said to be affected by an osteophyte if the MRI score > 0. A subregion is not affected by an osteophyte if that subregion is scored as 0.

Table 14.2.3.1
NRS Scores Observed and Change from Baseline Summary
ITT Population

Parameter = How Active the target knee arthritis has been

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
	n	nn		nn	nn
Visit 2	Mean	xx.x		xx.x	xx.x
MIV-711-	SD	xx.xx		xx.xx	xx.xx
201	Median	xx.x		xx.x	xx.x
DAY 1	Min	xx		xx	xx
	Max	xx		xx	xx
	n	nn	nn	nn	nn
VISIT 5	Mean	xx.x	xx.x	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx	xx.xx	xx.xx
201	Median	xx.x	xx.x	xx.x	xx.x
WEEK 8	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
	n	nn	nn	nn	nn
VISIT 6	Mean	xx.x	xx.x	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx	xx.xx	xx.xx
201	Median	xx.x	xx.x	xx.x	xx.x
WEEK 14	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
	n	nn	nn	nn	
VISIT 8	Mean	xx.x	xx.x	xx.x	
MIV-711-	SD	xx.xx	xx.xx	xx.xx	
201	Median	xx.x	xx.x	xx.x	
WEEK 26	Min	xx	xx	xx	
	Max	xx	xx	xx	

Table 14.2.3.1
NRS Scores Observed and Change from Baseline Summary
ITT Population

Parameter = How Active the target knee arthritis has been

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
VISIT 4 MIV-711-202 WEEK 40	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
VISIT 5 MIV-711-202 WEEK 52	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

Programming note: table will include summaries for following other NRS scores:

- Amount of pain severity in the target knee last week (SDTM: Overall pain severity in target knee
- Global Assessment Score: How active has the target knee arthritis has been in the past week (SDTM: How active was target knee arthritis)
- Satisfaction with target knee function (SDTM:How satisfied are you with target knee function)
- Worst pain severity in target knee (SDTM: Worst pain severity in target knee)
- Overall pain severity in other knee (SDTM: Overall pain severity in other knee)

Table 14.2.3.2
Statistical Analysis of NRS Scores, ITT Population

				Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
Endpoint	Group	Week	N	LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
xxxxx	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B
LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Programming notes:
Low pain scores are associated with a positive outcome (effect of drug).
For positive study expect large (negative changes) decreases from baseline by the time treatment reaches week 52.

Table will be expanded to include the analysis of the following NRS scores:

- Amount of Pain severity in the Target Knee Last Week
- Global Assessment Score: How active has the target knee arthritis has been in the past week (SDTM: How active was target knee arthritis)
- Satisfaction with target knee function (SDTM:How satisfied are you with target knee function)
- Worst pain severity in target knee (SDTM: Worst pain severity in target knee)
- Overall pain severity in other knee (SDTM: Overall pain severity in other knee)

Table 14.2.4.1
Normalized WOMAC Scores Observed and Change from Baseline Summary
ITT Population

Parameter = Normalized WOMAC Pain Score

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
	n	nn		nn	nn
Visit 2	Mean	xx.x		xx.x	xx.x
MIV-711-	SD	xx.xx		xx.xx	xx.xx
201	Median	xx.x		xx.x	xx.x
DAY 1	Min	xx		xx	xx
	Max	xx		xx	xx
	n	nn	nn	nn	nn
VISIT 5	Mean	xx.x	xx.x	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx	xx.xx	xx.xx
201	Median	xx.x	xx.x	xx.x	xx.x
WEEK 8	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
	n	nn	nn	nn	nn
VISIT 6	Mean	xx.x	xx.x	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx	xx.xx	xx.xx
201	Median	xx.x	xx.x	xx.x	xx.x
WEEK 14	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
	n	nn	nn	nn	
VISIT 8	Mean	xx.x	xx.x	xx.x	
MIV-711-	SD	xx.xx	xx.xx	xx.xx	
201	Median	xx.x	xx.x	xx.x	
WEEK 26	Min	xx	xx	xx	
	Max	xx	xx	xx	

Table 14.2.4.1
Normalized WOMAC Scores Observed and Change from Baseline Summary
ITT Population

Parameter = Normalized WOMAC Pain Score

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
VISIT 4 MIV-711-202 WEEK 40	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
VISIT 5 MIV-711-202 WEEK 52	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B
Normalized WOMAC PAIN Score = Total_WOMAC_Pain_50 x 2.
Normalized WOMAC Function Score = Total_WOMAC_Func_170 ÷ 1.7.
Normalized WOMAC stiffness Score = Total_WOMAC_stiff_20 x5.

Programming note: table will be expanded to include all Normalized WOMAC Pain scores, Normalized WOMAC Function score, Normalized WOMAC Stiffness scores

Programming note: similar table will be provided for the individual WOMAC scores
Table 14.2.4.2 Individual WOMAC Scores Observed and Change from Baseline Summary, ITT Population

Table 14.2.4.3
Statistical Analysis – Normalized WOMAC Scores, ITT Population

Parameter	Group	Week	N	Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
				LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
Pain Scores	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Progrmming note: table will be expanded to include Normalized WOMAC stiffness score and normalized WOMAC Difficulty score

Table 14.2.4.4
Statistical Analysis – WOMAC Pain Score (walking on a flat surface), ITT Population

				Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
Endpoint	Group	Week	N	LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
xxxxx	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Table 14.2.5
EQ-5D-5L Health Rating Score Response Observed and Change from Baseline Summary
ITT Population

Parameter = Mobility

Visit	Statistic	Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
		N = x	N = x	N = x	N = x
Visit 2 MIV-711-201	n	nn		nn	nn
	Mean	xx.x		xx.x	xx.x
	SD	xx.xx		xx.xx	xx.xx
	Median	xx.x		xx.x	xx.x
	Min	xx		xx	xx
	Max	xx		xx	xx
Visit 8 MIV-711-201	n	nn	nn	nn	
	Mean	xx.x	xx.x	xx.x	
	SD	xx.xx	xx.xx	xx.xx	
	Median	xx.x	xx.x	xx.x	
	Min	xx	xx	xx	
	Max	xx	xx	xx	
Visit 5 MIV-711-202	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

Programming note: table will be expanded to include all QOL variables:
Mobility, self-care, usual activity, pain or discomfort, and anxiety or depression, health rating score.

Table 14.2.6.1
E-Diary NRS Scores Observed and Change from Baseline Summary
ITT Population

Parameter = How would you rate overall pain severity over last 12 Hours?

			Group A N = x		Group B N = x	
			Observed	Change	Observed	Change
Endpoint	Visit	Statistic	N = x	N = x	N = x	N = x
AM Response	Visit 2 MIV-711-201 DAY 1	n	nn		nn	nn
		Mean	xx.x		xx.x	xx.x
		SD	xx.xx		xx.xx	xx.xx
		Median	xx.x		xx.x	xx.x
		Min	xx		xx	xx
		Max	xx		xx	xx
	VISIT 6 MIV-711-201 WEEK 14	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	VISIT 8 MIV-711-201 WEEK 26	n	nn	nn	nn	
		Mean	xx.x	xx.x	xx.x	
		SD	xx.xx	xx.xx	xx.xx	
		Median	xx.x	xx.x	xx.x	
		Min	xx	xx	xx	
		Max	xx	xx	xx	

Table 14.2.6.1
E-Diary NRS Scores Observed and Change from Baseline Summary
ITT Population

Parameter = How would you rate overall pain severity over last 12 Hours?

			Group A N = x		Group B N = x	
			Observed	Change	Observed	Change
Endpoint	Visit	Statistic	N = x	N = x	N = x	N = x
AM Response	VISIT 4 MIV-711-202 WEEK 40	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	VISIT 5 MIV-711-202 WEEK 52	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B

Programming note:

Table will be expanded to include the analysis of the following e-diary assessments:

- AM assessment
- PM assessment
- 24 Hour Overall Assessment

Table 14.2.6.2
Statistical Analysis of e-diary NRS Assessment, ITT Population

Endpoint	Group	Week	N	Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
				LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
AM Assessment	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		8 (V5: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B
LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Programming note:

Table will be expanded to include the PM assessment and 24 Hour Overall Assessment

Table 14.2.6.3
E-Diary Observed and Change from Baseline Summary of the Percentage of 'Yes' Scores for Analgesic Useage
ITT Population

			Group A N = x		Group B N = x	
			Observed	Change	Observed	Change
Endpoint	Visit	Statistic	N = x	N = x	N = x	N = x
AM Response	Visit 2 MIV-711-201 DAY 1	n	nn		nn	nn
		Mean	xx.x		xx.x	xx.x
		SD	xx.xx		xx.xx	xx.xx
		Median	xx.x		xx.x	xx.x
		Min	xx		xx	xx
		Max	xx		xx	xx
	VISIT 6 MIV-711-201 WEEK 14	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	VISIT 8 MIV-711-201 WEEK 26	n	nn	nn	nn	
		Mean	xx.x	xx.x	xx.x	
		SD	xx.xx	xx.xx	xx.xx	
		Median	xx.x	xx.x	xx.x	
		Min	xx	xx	xx	
		Max	xx	xx	xx	

Table 14.2.6.4
E-Diary Observed and Change from Baseline Summary of the Percentage of 'Yes' Scores for Analgesic Useage
ITT Population

			Group A N = x		Group B N = x	
			Observed	Change	Observed	Change
Endpoint	Visit	Statistic	N = x	N = x	N = x	N = x
AM Response	VISIT 4 MIV-711-202 WEEK 40	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	VISIT 5 MIV-711-202 WEEK 52	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 study for Group A and Group B
Table summarizes for those patients who responded Yes to the question: "Have you taken any pain medication over the last 12 hours since you last answered your OA Daily Diary?"

Programming note:

Table will be expanded to include the analysis of the following e-diary assessments:

- AM assessment
- PM assessment
- 24 Hour Overall Assessment

Table 14.2.6.65
E-Diary Pain Medication Usage Over Last 12 Hours
Number and Percentage of Patients with each Reported Severity Category
ITT Population

Endpoint	Visit	Category	Group A N = x	Group B N = x
		Number of Patients [1]	nn	nn
AM Assessment	Visit 2	Less than Normal	nn (nn.n%)	nn (nn.n%)
	MIV-711-201	Normal	nn (nn.n%)	nn (nn.n%)
	DAY 1	More than Normal	nn (nn.n%)	nn (nn.n%)
		Number of Patients [1]	nn	nn
	VISIT 6	Less than Normal	nn (nn.n%)	nn (nn.n%)
	MIV-711-201	Normal	nn (nn.n%)	nn (nn.n%)
	WEEK 14	More than Normal	nn (nn.n%)	nn (nn.n%)
		Number of Patients [1]	nn	nn
	VISIT 8	Less than Normal	nn (nn.n%)	nn (nn.n%)
	MIV-711-201	Normal	nn (nn.n%)	nn (nn.n%)
	WEEK 26	More than Normal	nn (nn.n%)	nn (nn.n%)
		Number of Patients [1]	nn	nn
	VISIT 4	Less than Normal	nn (nn.n%)	nn (nn.n%)
	MIV-711-202	Normal	nn (nn.n%)	nn (nn.n%)
	WEEK 40	More than Normal	nn (nn.n%)	nn (nn.n%)
		Number of Patients [1]	nn	nn
	VISIT 5	Less than Normal	nn (nn.n%)	nn (nn.n%)
	MIV-711-202	Normal	nn (nn.n%)	nn (nn.n%)
	WEEK 52	More than Normal	nn (nn.n%)	nn (nn.n%)

[1] indicates the number of patients with a YES response for each combination of visit and group
Programming note:
Table will be expanded to include the analysis of the following e-diary assessments:

- AM assessment
- PM assessment
- 24 Hour Overall Assessment

Table 14.2.7.1
Efficacy Biomarkers from Serum and Urine Samples - Summary of Observed and Change from Baseline Values
ITT Population

Parameter = Serum CTX-I

			Group A N = x		Group B N = x	
			Observed	Change	Observed	Change
AM/PM	Visit	Statistic	N = x	N = x	N = x	N = x
		n	nn		nn	nn
	Visit 2	Mean	xx.x		xx.x	xx.x
	MIV-711-	SD	xx.xx		xx.xx	xx.xx
	201	Median	xx.x		xx.x	xx.x
	DAY 1	Min	xx		xx	xx
		Max	xx		xx	xx
		n	nn	nn	nn	nn
	VISIT 4	Mean	xx.x	xx.x	xx.x	xx.x
	MIV-711-	SD	xx.xx	xx.xx	xx.xx	xx.xx
	201	Median	xx.x	xx.x	xx.x	xx.x
	WEEK 4	Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
		n	nn	nn	nn	nn
	VISIT 6	Mean	xx.x	xx.x	xx.x	xx.x
	MIV-711-	SD	xx.xx	xx.xx	xx.xx	xx.xx
	201	Median	xx.x	xx.x	xx.x	xx.x
	WEEK 14	Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	Etc....					

Baseline is defined as: Visit 2 in the MIV-711-201 for Group, Visit 2 in the MIV-711-202 for Group B

Programming note: table will include parameters Serum CTX-I and urine CIX-II

Table 14.2.7.1
Efficacy Biomarkers from Serum and Urine Samples - Summary of Observed and Change from Baseline Values
ITT Population

Parameter = Serum CTX-I

			Group A N = x		Group B N = x	
			Observed	Change	Observed	Change
AM/PM	Visit	Statistic	N = x	N = x	N = x	N = x
AM Response	VISIT 8 MIV-711-201 WEEK 26	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	VISIT 2 MIV-711-202 WEEK 27	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	VISIT 4 MIV-711-202 WEEK 40	n	nn	nn	nn	nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx
	VISIT 5 MIV-711-202 WEEK 52	n	nn	nn	nn	Nn
		Mean	xx.x	xx.x	xx.x	xx.x
		SD	xx.xx	xx.xx	xx.xx	xx.xx
		Median	xx.x	xx.x	xx.x	xx.x
		Min	xx	xx	xx	xx
		Max	xx	xx	xx	xx

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B

Programming note: table will include parameters Serum CTX-I and urine CIX-II

Table 14.2.7.2
Time-Integrated Concentrations (TIC) and Their Z-scores for Efficacy Biomarkers from Serum and Urine Samples
Summary of Observed Values
ITT Population

Parameter = TIC Serum CTX-I

Statistic	Group A N = x	Group B N = x
n	nn	nn
Mean	xx.x	xx.x
SD	xx.xx	xx.xx
Median	xx.x	xx.x
Min	xx	xx
Max	xx	xx

Programming note: table will include parameters TIC Serum CTX-I, TIC urine CIX-II, Z-Score Serum CTX-I, Z-Score urine CIX-II

Table 14.2.7.3
Statistical Analysis – Efficacy Biomarkers from Serum CIX-I and Urine CIX-II Samples, ITT Population

Parameter	Group	Week	N	Estimated Mean Level		Estimated Change from Visit 2 Study MIV-711-201	
				LS Mean	95% CI	LS Mean Difference from V2 MIV-711-201	95% CI
Serum CIX-I	A	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		4 (V4: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V2: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
	B	1 (V2: 201)	nn	xx.xx	(x.xx, x.xx)		
		4 (V4: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		14 (V6: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V8: 201	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		26 (V2: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		40 (V4: 202)	nn	xx.xx	(x.xx, x.xx)	xx.xx	(x.xx, x.xx)
		52 (V5: 202)	nn	xx.xx	(xx.x, xx.x)	xx.xx	(x.xx, x.xx)
Etc…							

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B

LS Mean = least squares mean, N denotes the number of Patients for each level of treatment used to estimate the LS means.

Programming note: table will be expanded to include urine CIX-II

Table 14.2.8.1
Brief Medication Questionnaire - Number and Percentage of Patients with each Medication Used by Visit
ITT Population

Medication	Visit	Group A N = x	Group B N = x
Medication 1		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
Medication 2		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
Etc..			

Table is sorted by descending frequency count of medication.

Table 14.2.8.2
Brief Medication Questionnaire - Number and Percentage of Patients with each Indication by Visit
ITT Population

Indication	Visit	Group A N = x	Group B N = x
Indication 1		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
Indication 2		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
Etc..			

Table is sorted by descending frequency count of indication

Table 14.2.8.3
Brief Medication Questionnaire - Number and Percentage of Patients with each Medication by Indication and Visit
PPS Population

Medication	Visit	Group A N = x	Group B N = x
Indication 1		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
Indication 2		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
		nn (nn.n%)	nn (nn.n%)
Etc..			

Table 14.2.8.4
Brief Medication Questionnaire - Compliance
Number and Percentage of Patients Who Missed Taking their Medication by Visit
ITT Population

Medication Name	How many times did you miss taking it?	Visit	Group A N = x	Group B N = x
	0		nn (nn.n%)	nn (nn.n%)
	1		nn (nn.n%)	nn (nn.n%)
	2		nn (nn.n%)	nn (nn.n%)
	3			
	Etc..			

Table 14.3.1.1
Summary of Treatment Emergent Adverse Events
SAF Population

	MIV-711-201			MIV-711-202		
	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x
All AEs	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E
'Related' AEs	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E
Mild AEs	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E
Moderate AEs	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E
Severe AEs	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E
Deaths	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E
Serious AEs	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E
AEs Leading to early discontinuation from study	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E	nn (nn.n%) E

TEAE = Treatment Emergent Adverse Event
nn = Number of Patientswith TEAEs
N = Number of PatientsExposed
(nn.n%) = nn/N x 100
E = Number of AEs

Table 14.3.1.2
Number and Percentage of Patients with Treatment Emergent Adverse Events
by System Organ Class, Preferred Term, and Group
SAF Population

	MIV-711-201			MIV-711-202		
System Organ Class Preferred Term	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x
System Organ Class 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
System Organ Class 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Table 14.3.1.3
Number and Percentage of Patients with Treatment Emergent Adverse Events 'Related to IMP'
by System Organ Class, Preferred Term, Severity, and Group
SAF Population

		MIV-711-201			MIV-711-202		
System Organ Class Preferred Term	Severity	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x
System Organ Class 1	Mild	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Moderate	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Severe	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	Mild	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Moderate	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Severe	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	Mild	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Moderate	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Severe	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
System Organ Class 2	Mild	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Moderate	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Severe	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	Mild	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Moderate	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Severe	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	Mild	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Moderate	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Severe	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

For patients with multiple adverse events of the same preferred term and different severities, the AE with the highest assessment of severity was used in the summary table.

Table 14.3.1.4
Number and Percentage of Patients with Serious Treatment Emergent Adverse Events
by System Organ Class, Preferred Term, and Group
SAF Population

	MIV-711-201			MIV-711-202		
System Organ Class Preferred Term	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x
System Organ Class 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
System Organ Class 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Table 14.3.1.5
Number and Percentage of Patients with Treatment Emergent Adverse Events Leading to Discontinuation
by System Organ Class, Preferred Term, and Group
SAF Population

	MIV-711-201			MIV-711-202		
System Organ Class Preferred Term	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x
System Organ Class 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
System Organ Class 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Table 14.3.1.6
Number and Percentage of Patients with Treatment Emergent Adverse Events by Frequency, Preferred Term, and Group
SAF Population

	MIV-711-201			MIV-711-202		
Preferred Term	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x	Group A 26 weeks N = x	Group B 26 weeks N = x	Overall N = x
Preferred Term 1	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 2	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term 3	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
Preferred Term xx	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Table 14.3.2.1
Clinical Laboratory Chemistry - Summary of Observed Values
SAF Population

Lab Parameter = *Lab Parameter (unit)*

Visit	Statistic	Group A N = x	Group B N = x
	n	nn	nn
VISIT 1	Mean	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx
201	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx
	n	nn	nn
VISIT 2	Mean	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx
201	Median	xx.x	xx.x
DAY 1	Min	xx	xx
	Max	xx	xx
	n	nn	nn
VISIT 3	Mean	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx
201	Median	xx.x	xx.x
WEEK 2	Min	xx	xx
	Max	xx	xx
Etc…			

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B

Medivir
Protocol Number: MIV-711-202

Table 14.3.2.2
Clinical Laboratory Hematology - Summary of Observed Values
SAF Population

Lab Parameter = *Lab Parameter (unit)*

Visit	Statistic	Group A N = x	Group B N = x
	n	nn	nn
VISIT 1	Mean	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx
201	Median	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx
	n	nn	nn
VISIT 2	Mean	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx
201	Median	xx.x	xx.x
DAY 1	Min	xx	xx
	Max	xx	xx
	n	nn	nn
VISIT 3	Mean	xx.x	xx.x
MIV-711-	SD	xx.xx	xx.xx
201	Median	xx.x	xx.x
WEEK 2	Min	xx	xx
	Max	xx	xx
Etc…			

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B

Table 14.3.2.3
Clinical Laboratory Chemistry – Shift From Baseline to Maximum Value
SAF Population

Lab Parameter = *Lab Parameter (unit)*

Group	Maximum Value	Baseline Low	Baseline Normal	Baseline High
A	Low	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Normal	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	High	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
B	Low	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Normal	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	High	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B
Note that the maximum is taken over the visits post first MIV-711 dose. Thus, the number of vists the maximum is taken over will not be the same for Group A and Group B.

Table 14.3.2.4
Clinical Laboratory Chemistry – Shift From Baseline to Minimum Value
SAF Population

Lab Parameter = *Lab Parameter (unit)*

Group	Minimum Value	Baseline		
		Low	Normal	High
A	Low	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Normal	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	High	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
B	Low	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	Normal	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)
	High	nn (nn.n%)	nn (nn.n%)	nn (nn.n%)

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B
Note that the minimum is taken over the visits post first MIV-711 dose.
Thus, the number of vists the minimum is taken over will not be the same for Group A and Group B.

Programming Note: Similar tables will be created for hematology parameters:
Table 14.3.2.5 Clinical Laboratory Hematology – Shift From Baseline to Maximum Value, SAF Population
Table 14.3.2.6 Clinical Laboratory Hematology – Shift From Baseline to Minimum Value, SAF Population

Table 14.3.3
Vital Signs Blood Pressure and Heart Rate Summary of Observed and Change from Baseline Values
SAF Population

Parameter = Systolic Blood Pressure (mmHg)

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
VISIT 1 MIV-711-201 SCREENING	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
VISIT 2 MIV-711-201 DAY 1	n	nn		nn	nn
	Mean	xx.x		xx.x	xx.x
	SD	xx.xx		xx.xx	xx.xx
	Median	xx.x		xx.x	xx.x
	Min	xx		xx	xx
	Max	xx		xx	xx
VISIT 3 MIV-711-201 WEEK 2	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
Visit 4 MIV- 711-201 WEEK 3	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
Etc…					

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B.
Programming Notes: Table will be expanded to include diastolic blood pressure and heart rate, subject weight.

Table 14.3.4.1
12 Lead ECG – Summary of Observed and Change from Baseline Values
SAF Population

Parameter = QT Interval *(msec)*

		Group A N = x		Group B N = x	
		Observed	Change	Observed	Change
Visit	Statistic	N = x	N = x	N = x	N = x
VISIT 1 MIV-711-201 SCREENING	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
VISIT 2 MIV-711-201 DAY 1	n	nn		nn	nn
	Mean	xx.x		xx.x	xx.x
	SD	xx.xx		xx.xx	xx.xx
	Median	xx.x		xx.x	xx.x
	Min	xx		xx	xx
	Max	xx		xx	xx
VISIT 3 MIV-711-201 WEEK 2	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
Visit 4 MIV- 711-201 WEEK 3	n	nn	nn	nn	nn
	Mean	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x
	Min	xx	xx	xx	xx
	Max	xx	xx	xx	xx
Etc…					

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B
QTcB = QT corrected according to Bazett, QTcF = QT corrected according to Fridericia.

Table 14.3.4.2
12 Lead ECG – Categorical Summary of Observed Values
SAF Population

Parameter = QT (msec)

Visit	Category (unit)	Group A N = x	Group B N = x
VISIT 1 MIV-711-201 SCREENING	≤ 450	nn (nn.n%)	nn (nn.n%)
	450 < to ≤ 480	nn (nn.n%)	nn (nn.n%)
	480 < to ≤ 500	nn (nn.n%)	nn (nn.n%)
	>500	nn (nn.n%)	nn (nn.n%)
VISIT 2 MIV-711-201 DAY 1	≤ 450	nn (nn.n%)	nn (nn.n%)
	450 < to ≤ 480	nn (nn.n%)	nn (nn.n%)
	480 < to ≤ 500	nn (nn.n%)	nn (nn.n%)
	>500	nn (nn.n%)	nn (nn.n%)
VISIT 3 MIV-711-201 WEEK 2	≤ 450	nn (nn.n%)	nn (nn.n%)
	450 < to ≤ 480	nn (nn.n%)	nn (nn.n%)
	480 < to ≤ 500	nn (nn.n%)	nn (nn.n%)
	>500	nn (nn.n%)	nn (nn.n%)
Etc…			

Baseline is defined as: Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 2 in the MIV-711-202 for Group B

QTcB = QT corrected according to Bazett, QTcF = QT corrected according to Fridericia.

Programming note: Table will include: QTcB interval and QTcF interval

Table 14.3.4.3
12 Lead ECG – Categorical Summary of Change from Baseline
SAF Population

Parameter = QT (msec)

Visit	Category (unit)	Group A N = x	Group B N = x
VISIT 1 MIV-711-201 SCREENING	<= 0	nn (nn.n%)	nn (nn.n%)
	>0 to ≤ 30	nn (nn.n%)	nn (nn.n%)
	>30 to ≤ 60	nn (nn.n%)	nn (nn.n%)
	>60	nn (nn.n%)	nn (nn.n%)
VISIT 2 MIV-711-201 DAY 1	<= 0	nn (nn.n%)	nn (nn.n%)
	>0 to ≤ 30	nn (nn.n%)	nn (nn.n%)
	>30 to ≤ 60	nn (nn.n%)	nn (nn.n%)
	>60	nn (nn.n%)	nn (nn.n%)
Etc…			

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

QTcB = QT corrected according to Bazett, QTcF = QT corrected according to Fridericia.

Programming note: Table will include: QTcB interval and QTcF interval

15. Listing Shells

Listing 16.2.1.1
Patient Disposition

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Completion Status	If Discontinued, Day of Withdrawal	If Discontinued, Date of Withdrawal	Reason For Discontinuation
		Completed			
		Discontinued			

Listing 16.2.1.2
Patients Excluded from the Analysis Populations

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Population	Reason for Exclusion
		PPS	
		ITT	

Listing 16.2.1.3
Enrolled Patients Who Did Not Meet All Eligibility Criteria

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Criteria Category	Criteria Description	Response
		Inclusion		No
		Exclusion		Yes

Listing 16.2.1.4
Exclusion Tests
FSH test, Serology, Urine Drug Screen

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Exclusion Test	Result	Units
					FSH test		
					Etc...		

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Listing 16.2.2.1
Protocol Deviations

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Study Day	Time Point	Date Deviation Occurred	Category	Explanation	Classification
					Time Window		Minor
					Dosing		Major
					Exclusion Tests		Major
					Etc…		

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Listing 16.2.4.1
Demographics

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Gender	Ethnicity	Race	Age (yrs)	Height (cm)	Weight (kg)	BMI (kg/m^2)

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Listing 16.2.4.2
Medical History

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Reported Term >MedDRA Preferred Term >>System Organ Class	Onset Date	Status	Recovered Date	Currently Treated with Medication?
				Ongoing		Yes/No

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Listing 16.2.5.1
Prior and Concomitant Medications

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Medication Name >WHO Drug Name >>ATC Classification >>>ATC Code >>>>ATC Dictionary Text	Category	Start Date	Stop Date	Ongoing?	Dose/ Unit	Frequency	Route	Indication	Was There an AE	Pain Medication
			Prior CM				Yes/No					Yes/No

Programming note: Pain Medication = 'Yes' if ATC = 'ANALGESICS'

Listing 16.2.5.2
Dose Administration at Clinic Visits

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Dose	Time of Dose	Dose Form / Route

Listing 16.2.5.3
Dose Administration Compliance, ITT Population

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Dose	Dispensed Amount (Capsules)	Returned Amount (Capsules)	Actual Number of Capsules Used	Were all unused Capsules returned?	Reason not all unused Capsules returned	Medication error	Number of Actual Days exposed to IMP

The 'actual number of capsules used' was derived as the 'number of capsules dispensed' minus the 'number of capsules returned'.
'Number of actual days exposed to IMP' is the number of days of actual dose exposure from V2 (first dose) to V5 (last dose), since each patient is to receive 1 capsule of dosing per day of dose administration.
Withdrawn patients are not included in this listing.

Listing 16.2.5.4
Dose Administration Overall Compliance at Visit 5, ITT Population

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Dose	Total Dispensed Amount (Capsules) [1]	Total Returned Amount (Capsules) [2]	Total Actual Number of Capsules Used	Total Number of Days exposed to IMP	Overall IMP Compliance

[1] obtained as the total number over visits 2, 4.
[2] obtained as the total number over visits 4, 5.

The 'Total actual number of capsules used' was derived as the 'Total number of capsules dispensed' minus the 'Total number of capsules returned'.
Overall IMP compliance: (Total actual number of capsules used / Total number of days exposed to IMP) x 100%
Withdrawn patients are not included in this listing.

Listing 16.2.6.1
Numerical Rating Scale of Knee Pain (One Week Recall)

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Assessment	Target Knee Used for NRS	Overall Pain Severity in Target Knee	Worst Pain Severity Target Knee	Overall Pain Severity in Other Knee	Global Disease Activity	Satisfied with Target Knee Function

Listing 16.2.6.2
Numerical Rating Scale of Knee Pain Change From Baseline (One Week Recall)

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Assessment	Target Knee Used for NRS	Overall Pain Severity in Target Knee	Worst Pain Severity Target Knee	Overall Pain Severity in Other Knee	Global Disease Activity	Satisfied with Target Knee Function

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Listing 16.2.6.3
Imaging Results Imorphics - MRI of Bone Area for the Target Knee
Observed and Change from Baseline

Study Group = Group A

				Area of bone in the medial femur region, MF	
Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Assessment	Score	Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: source data obtained from Imorphics: Area of bone in the medial femur region, MF (MF_TAB)

Listing 16.2.6.4
Imaging Results Imorphics - MRI of Cartilage Thickness for the Target Knee
Observed and Change from Baseline

Study Group = Group A

				Average thickness of cartilage in the central medial femur region		Average thickness of cartilage in the central medial tibia region	
Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Assessment	Score	Change Score	Score	Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: source data obtained from Imorphics variables:
Average thickness of cartilage in the central medial femur region (CM_FEMUR_THCTAB)
Average thickness of cartilage in the central medial tibia region (CM_TIBIA_THCTAB)

Listing 16.2.6.5
Imaging Results Imorphics – Total BML Volume
Observed and Change from Baseline

Study Group = Group A

					Combined volume of all BML regions
Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Assessment	Score	Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: source data obtained from Imorphics:
Combined volume of all BML regions (TOTAL_BML_VOLUME)

Listing 16.2.6.7.1
Other Imaging variables - Imorphics Bone Area

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Imorphics 1 Score	Imorphics 1 Change Score	Imorphics 2 Score	Imorphics 2 Change Score	Imorphics 3 Score	Imorphics 3 Change Score	Imorphics 4 Score	Imorphics 4 Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: Imorphics tests will include:

Area of bone in the lateral femur region, LF (LF_TAB)
Area of bone in the medial tibia region, MT (MT_TAB)
Area of bone in the lateral femur region, LT (LT_TAB)
Area of bone in the medial patella region, MP (MP_TAB)
Area of bone in the lateral patella region, LP (LP_TAB)

Listing 16.2.6.7.2
Other Imaging variables - Imorphics Bone 3D Shape

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Imorphics 1		Imorphics 2		Imorphics 3		Imorphics 4	
				Score	Change Score	Score	Change Score	Score	Change Score	Score	Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: Imorphics tests will include:
Distance along the femur 3D OA bone shape vector 0 is defined as the mean shape of a population of knees without osteoarthritis, units are 1 Standard Deviation of population of healthy knees. Likely range -2 to +8 (FEMUR_3D_VECTOR)
Distance along the tibia 3D OA bone shape vector (TIBIA_3D_VECTOR)
Distance along the patella 3D OA bone shape vector (PATELLA_3D_VECTOR)

Listing 16.2.6.7.3
Other Imaging variables - Imorphics Cartilage Thickness

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201 Visit	Collection Date	Imorphics 1 Score	Imorphics 1 Change Score	Imorphics 2 Score	Imorphics 2 Change Score	Imorphics 3 Score	Imorphics 3 Change Score	Imorphics 4 Score	Imorphics 4 Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: Imorphics tests will include:

Average thickness of cartilage in the central lateral femur region (CL_FEMUR_THCTAB)
Average thickness of cartilage in the central lateral tibia region (CL_TIBIA_THCTAB)
Average thickness of cartilage in the trochlear femur region (TR_FEMUR_THCTAB)
Average thickness of cartilage in the patella region (PATELLA_THCTAB)

Listing 16.2.6.7.4
Other Imaging variables - Imorphics Cartilage Denudation

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Imorphics 1 Score	Imorphics 1 Change Score	Imorphics 2 Score	Imorphics 2 Change Score	Imorphics 3 Score	Imorphics 3 Change Score	Imorphics 4 Score	Imorphics 4 Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: Imorphics tests will include:
Denuded area of cartilage in the central medial femur region (CM_FEMUR_DAB)
Denuded area of cartilage in the central medial tibia region (CM_TIBIA_DAB)
Denuded area of cartilage in the central lateral femur region (CL_FEMUR_DAB)
Denuded area of cartilage in the central lateral tibia region (CL_TIBIA_DAB)
Denuded area of cartilage in the trochlear femur region (TR_FEMUR_DAB)
Denuded area of cartilage in the patella (PATELLA_DAB)

Listing 16.2.6.7.5
Other Imaging variables - Imorphics Cartilage Reference Bone Area

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Imorphics 1		Imorphics 2		Imorphics 3		Imorphics 4	
				Score	Change Score	Score	Change Score	Score	Change Score	Score	Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: Imorphics tests will include:
Total area of the central medial femur region (CM_FEMUR_TAB)
Total area of the central medial tibial region (CM_TIBIA_TAB)
Denuded area of cartilage in the central lateral femur region (CL_FEMUR_TAB)
Total area of the central lateral tibial region (CL_TIBIA_TAB)
Denuded area of cartilage in the trochlear femur region (TR_FEMUR_TAB)
Denuded area of cartilage in the patella (PATELLA_TAB)

Listing 16.2.6.7.6
Other Imaging variables - Imorphics BML volume

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201 Visit	Collection Date	Imorphics 1 Score	Imorphics 1 Change Score	Imorphics 2 Score	Imorphics 2 Change Score	Imorphics 3 Score	Imorphics 3 Change Score	Imorphics 4 Score	Imorphics 4 Change Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Programming note: Imorphics tests will include:
BML volume in medial femur, MF region (Figure 3) (MF_BML_VOLUME)
BML volume in lateral femur, LF region (LF_BML_VOLUME)
BML volume in trochlear femur, TrF region (TRF_BML_VOLUME)
BML volume in medial tibia, MT region (MT_BML_VOLUME)
BML volume in lateral tibia, LT region (LT_BML_VOLUME)
BML volume in patella, P region (P_BML_VOLUME)

Listing 16.2.6.7.7
Other Imaging variables - Imorphics Combined

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Overall Knee Change, Compose of 3D Bone and Cartilage Thickness Score

Programming note: Imorphics tests will include:
Exploratory endpoint representing overall knee change, compose of 3D bone and cartilage thickness (INDEX_BONE_CARTILAGE)

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Listing 16.2.6.8.1
Other Imaging variables - MOAKS Bone Marrow Lesion (BML) and Cyst

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Laterality of Patient	Subcategory	MOAKS Test 1		MOAKS Test 2		MOAKS Test 3	
						Score	Score Text	Score	Score Text	Score	Score Text

Programming note: MOAKS tests will include:
Number of BMLs
% that is BML
Size of BML

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Listing 16.2.6.8.2
Other Imaging variables - MOAKS Cartilage Assessments

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Laterality of Patient	Subcategory	MOAKS Test 1		MOAKS Test 2	
						Score	Score Text	Score	Score Text

Programming note: MOAKS tests will include:
% Full Thickness Loss
Size of any cartilage loss

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Listing 16.2.6.8.3
Other Imaging variables - MOAKS Hoffa-Synovitis/Effusion-Synovitis

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Laterality of Patient	Subcategory	MOAKS Test 1		MOAKS Test 2	
						Score	Score Text	Score	Score Text

Programming note: MOAKS tests will include: Effusion-Synovitis, Hoffa-Synovitis

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Listing 16.2.6.8.4
Other Imaging variables - MOAKS Ligament Assessments

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Laterality of Patient	Subcategory	MOAKS Test 1		MOAKS Test 2		MOAKS Test 3	
						Score	Score Text	Score	Score Text	Score	Score Text

Programming note: MOAKS tests will include: ACL Repair, ACL Tears, Assoc wth BML/Cysts at site of insertion, PCL Tears, Patellar Tendon Signal

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Listing 16.2.6.8.5
Other Imaging variables - MOAKS Meniscus

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Laterality of Patient	Subcategory	MOAKS Test 1		MOAKS Test 2		MOAKS Test 3	
						Score	Score Text	Score	Score Text	Score	Score Text

Programming note: MOAKS tests will include: Lateral Meniscus: Anterior Extrusion, Lateral Meniscus: Lateral Extrusion, Medial Meniscus: Anterior Extrusion, Medial Meniscus: Medial Extrusion, Lateral Meniscus Anterior, Lateral Meniscus Body, Lateral Meniscus Posterior

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Listing 16.2.6.8.6
Other Imaging variables - MOAKS Osteophytes Assessments

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Laterality of Patient	Subcategory	MOAKS Test 1 Score	MOAKS Test 1 Score Text

Programming note: MOAKS tests will include: Osteophyte Size

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Listing 16.2.6.8.7
Other Imaging variables - MOAKS Periarticular Features

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Laterality of Patient	Subcategory	MOAKS Test 1		MOAKS Test 2		MOAKS Test 3	
						Score	Score Text	Score	Score Text	Score	Score Text

Programming note: MOAKS tests will include: Ganglion Cysts, Infrapatellar Bursae Signal, Pes Anserine bursitis, Prepatellar Bursae Signal, Iliotibial Band Signal, Loose Bodies,Popliteal Cyst

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Listing 16.2.6.9
Observed Raw ICOAP Scores

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Assessment	Time of Assessment	IP1	IP2	IP3	IP4	IP5	IP6	IP7	IP8	IP9	IP10	IP11
		VISIT 2 BASELINE DAY													
		VISIT 5 WEEK 8													
		VISIT 6 WEEK 14													
		Etc…													

Listing 16.2.6.10
Transformed ICOAP Scores

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date of Assessment	Time of Assessment	Constant Pain Subscale		Intermittent pain subscale		Total pain score	
					Observed	Change	Observed	Change	Observed	Change
		VISIT 2 BASELINE								
		DAY								
		VISIT 5 WEEK 8								
		VISIT 6 WEEK 14								
		Etc…								

Listing 16.2.6.11
Western Ontario and McMaster Index (WOMAC) - Pain Questions

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	Walking on a Flat Surface	Going Up or Down Stairs	at Night While in Bed	Sitting or Lying Down	While Standing

Listing 16.2.6.12
Western Ontario and McMaster Index (WOMAC) – Stiffness Questions

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	Stiffness after First Woke Up in Morning	Stiffness Sitting or Lying Down

Listing 16.2.6.13
Western Ontario and McMaster Index (WOMAC) - Difficulty Questions

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	When going Down the Stairs	When Going Up the Stairs	Getting Up from a sitting	While Standing	When Bending to the Floor	Walking on a Flat Surface

Programming note: listing will be expanded to show all 17 difficulty questions

Listing 16.2.6.14
Western Ontario and McMaster Index (WOMAC)
Derived Scores and Change from Baseline

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Total WOMAC Pain Score [1]	Total WOMAC Function Score [2]	Total WOMAC Stiffness Score [3]	Normalized WOMAC Pain Score	Change from Baseline Normalized WOMAC Pain Score	Normalized WOMAC Function Score	Change from Baseline Normalized WOMAC Function Score	Normalized WOMAC Stiffness Score	Change from Baseline Normalized WOMAC Stiffness Score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

[1] Total WOMAC Pain Score (Total_WOMAC_Pain_50): sum of the 5 WOMAC pain responses
[2] Total WOMAC Function Score (Total_WOMAC_Func_170): sum of the 17 WOMAC function responses
[3] Total WOMAC Stiffness Score (Total_WOMAC_stiff_2): sum of the 2 WOMAC stiffness responses

WOMAC PAIN Score 100 = Total_WOMAC_Pain_50 x 2.
WOMAC Function Score 100 = Total_WOMAC_Func_170 ÷ 1.7.
WOMAC stiffness Score 100 = Total_WOMAC_stiff_2 ÷ 0.2.

Listing 16.2.6.15
OARSI-OMERACT Responder Index

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Total WOMAC Pain Score [1]	Total WOMAC Function Score [2]	Normalized WOMAC Pain Score	Normalized WOMAC Function Score	Normalized Global Assessment NRS
		Visit 2					
		Visit 8					

[1] Total WOMAC Pain Score (Total_WOMAC_Pain_50): sum of the 5 WOMAC pain responses
[2] Total WOMAC Function Score (Total_WOMAC_Func_170): sum of the 17 WOMAC function responses
Global Assessment NRS = "How Active Target Knee Arthritis Has Been", from Listing 16.2.6.1
Normalized WOMAC PAIN Score = Total_WOMAC_Pain_50 x 2.
Normalized WOMAC Function Score = Total_WOMAC_Func_170 ÷ 1.7.
Normalized Global Assessment NRS = (Global Assessment NRS) x 10.

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Listing 16.2.6.16
OARSI-OMERACT Responder Index
Change from Baseline and Percentage Change from Baseline Scores

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Score	Change from Baseline	Percent Change from Baseline	Criteria (1, 2)	Response Criteria (1, 2)	Criteria (3,4,5)	Response Criteria (3,4,5)	Responder
101			xx	yy	1	Yes	3	NA	No
101			xx	yy	2	No	4	NA	
101			xx	yy			5	NA	
102			xx	yy	1	No	3	Yes	Yes
102			xx	yy	2	No	4	Yes	
102			xx	yy			5	No	
103			xx	yy	1				Yes
103			xx	yy	2				
103			xx	yy			5		
104			xx	yy			3		
104			xx	yy			4		
104			xx	yy					
105			xx	yy					
105			xx	yy			4		
105			xx	yy					

Percent Change from Baseline: ((Visit 5 Score – Baseline Score) ÷ Baseline Score) x 100

Criteria 1: WOMAC Pain: decrease from baseline >=20 and **Percentage Decrease from Baseline >=50%**

Criteria 2: WOMAC Function: decrease from baseline >=20 and **Percentage Decrease from Baseline >=50%**

Criteria 3: WOMAC Pain: decrease from baseline >=10 and **Percentage Decrease from Baseline >=20%**

Criteria 4: WOMAC Function: decrease from baseline >=10 and **Percentage Decrease from Baseline >=20%**

Criteria 5: Global Assessment: decrease from baseline >=10 and **Percentage Decrease from Baseline >=20%**

A subject is a 'Yes' responder if either of criteria 1 or 2 are satisfied. If neither criteria 1 or 2 are satisfied, criteria 3, 4 and 5 will be checked. A subject is a 'Yes' responder if at least 2 of these 3 criteria (3, 4, 5) are satisfied.
Programming notes: Criteria column will be flagged with the number 1, 2, 3, 4, 5 only if the conditions for that criteria are satisfied. Criteria 3, 4, 5 will be shown only if Criteria 1 and 2 have been checked and neither of these initial two conditions are satisfied.

Listing 16.2.6.17
Global Improvements

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	Knee problem	Knee Pain	Knee Function

Listing 16.2.6.18
Quality of Life Patient Reported Outcomes - EQ-5D-5L

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	Mobility	Self-care	Usual activity	Pain or Discomfort	Anxiety or depression	Health rating score

For questions on Mobility, Self-care, Usual Activity, Pain or discomfort, and Anxiety or Depression higher scores indicate worse quality of life.
The Health Rating Score is a VAS score ranging from 0 to 100 such that higher scores are associated with improved health and better quality of life.

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Listing 16.2.6.19
Quality of Life Patient Reported Outcomes Change from Baseline Scores - EQ-5D-5L

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	Mobility	Self-care	Usual activity	Pain or Discomfort	Anxiety or depression	Health rating score

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

For questions on Mobility, Self-care, Usual Activity, Pain or discomfort, and Anxiety or Depression higher scores indicate worse quality of life.

The Health Rating Score is a VAS score ranging from 0 to 100 such that higher scores are associated with improved health and better quality of life.

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Listing 16.2.6.20
Brief Medication Questionnaire

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	Question	Response
				How much did you take each time	
				How many days did you take it	
				The dosage times are inconvenient	
				Etc…	

Listing 16.2.6.21
E-Diary Assessments over the Last 12 Hours

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Study Day	Date Of Assessment	Time Point	Pain Medication Use Over Last 12 Hours?	Severity Pain Medication Usage Over last 12 Hours	NRS: Overall Pain Severity in Target Knee Over Last 12 Hours
				AM			
				PM	YES	Less than Normal	
					NO	Normal	
						More than normal	

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Listing 16.2.6.22
E-Diary Assessments – Derived Results for each Study Visit

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Time Point	Percentage of Patients who used Pain medication use over last 12 hours?	Change from Baseline percentage of 'Yes' scores for analgesic use	Severity Pain medication usage over last 12 hours [2]	NRS: Overall pain severity in target knee over last 12 hours [3]	Change from Baseline NRS
xxxxxx		Baseline	AM	xx.x				
		Visit 4	AM	xx.x	xx.x	Less than Normal		
		Visit 5	AM	xx.x	xx.x	Normal		
		Baseline	PM			More than normal		
		Visit 4	PM					
		Visit 5	PM					
		Baseline	Overall					
		Visit 4	Overall					
		Visit 5	Overall					

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B
[1] Denominator for AM, PM calculations is the actual number of days assessed, where the number of days >=10 days and <= 14 days. The overall percentage combining AM and PM measures:
Overall percentage = (xx/AM denominator + yy/PM denominator)/2, where 'xx' = count of AM 'Yes', 'yy' = count of PM 'Yes'.
[2] Derived results were considered only for YES responses in [1]. For those cases the worst response over the interval of all responses for each visit was interpreted as the derived response for that Visit.
[3] the derived NRS score for each Visit was obtained as the arithmetic mean (the average) of all scores recorded within the identified interval for that Visit.

Listing 16.2.6.23
Efficacy Biomarkers from Serum and Urine Samples

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date Of Assessment	Serum CTX-I (ug/L)	Serum CTX-I Change from Baseline (ug/L)	Urine CTX-II (ug/L)	Urine Creatinine (mmol/L)	Urine CTX-II /Creat (ng/mmoL)	Urine CTX-II /Creat Change from Baseline (ng/mmoL)

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

Listing 16.2.6.24
Time-Integrated Concentrations (TIC) and Their Z-scores
for Efficacy Biomarkers from Serum and Urine Samples

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	TIC Serum CTX-I (ug/L)	TIC Urine CTX-II /Creat (ng/mmoL)	Z-Score Serum CTX-I	Z-Score Urine CTX-II/Creat

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Listing 16.2.7.1
Adverse Events

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Adverse Event >MedDRA Preferred Term >>System Organ Class	Start Date Time	Stop Date Time	Seri-ous	Outcome	Severity	Action Taken Study Medica-tion [1]	Relation-ship to Study Medica-tion	AE Start Time from First Dose (day)

[1] Action taken results that state 'MEDICATION' indicate a concomitant medication was administered. No action was taken with respect to study medication unless specifically stated otherwise

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Listing 16.2.7.2
Serious Adverse Events

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Adverse Event >MedDRA Preferred Term >>System Organ Class	Start Date Time	Stop Date Time	Outcome	Severity	Action Taken Study Medication [1]	Relationship to Study Medication	AE Start Time from First Dose (day)

[1] Action taken results that state 'MEDICATION' indicate a concomitant medication was administered. No action was taken with respect to study medication unless specifically stated otherwise

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Listing 16.2.7.3
Adverse Events Leading To Discontinuation

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Adverse Event >MedDRA Preferred Term >>System Organ Class	Start Date Time	Stop Date Time	Seri-ous	Outcome	Severity	Action Taken Study Medica-tion [1]	Relation-ship to Study Medica-tion	AE Start Time from First Dose (day)

[1] Action taken results that state 'MEDICATION' indicate a concomitant medication was administered. No action was taken with respect to study medication unless specifically stated otherwise

Listing 16.2.8.1
Clinical Laboratory Chemistry - Observed Values

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Lab Parameter 1 (unit) Result/*Flag*	Lab parameter 2 (unit) Result/*Flag*	Lab parameter 3 (unit) Result/*Flag*	Lab parameter 4 (unit) Result/*Flag*

H=High, L=Low, CS=Clinically Significant, NCS=Not Clinically Significant

Programming Note: If Flag is present (H or L), clinical significance will be identified by one of 'NCS' or 'CS'.

Listing 16.2.8.2
Clinical Laboratory Hematology - Observed Values

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Lab Parameter 1 (unit)	Lab parameter 2 (unit)	Lab parameter 3 (unit)	Lab parameter 4 (unit)
					Result/*Flag*	Result/*Flag*	Result/*Flag*	Result/*Flag*

H=High, L=Low, CS=Clinically Significant, NCS=Not Clinically Significant

Programming Note: If Flag is present (H or L), clinical significance will be identified by one of 'NCS' or 'CS'.

Listing 16.2.8.3
Clinical Laboratory Urinalysis - Observed Values

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Lab Parameter 1 (unit)	Lab parameter 2 (unit)	Lab parameter 3 (unit)	Lab parameter 4 (unit)
					Result/*Flag*	Result/*Flag*	Result/*Flag*	Result/*Flag*

H=High, L=Low, AB=Abnormal, CS=Clinically Significant, NCS=Not Clinically Significant

Programming Note: If Flag is present (H, L, or AB), clinical significance will be identified by one of 'NCS' or 'CS'.

Listing 16.2.8.4
Clinical Laboratory Urinalysis – Positive Microscopic Findings

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Test Name	Result	Unit	Flag	Clinical Significance

*H=High, L=Low, AB=Abnormal, CS=Clinically Significant, NCS=Not Clinically Significant

Programming Note: If Flag is present (H, L, or AB), clinical significance will be identified by one of 'NCS' or 'CS'.

Listing 16.2.8.5
Vital Signs – Observed Values

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Supine Heart Rate (beats/min)	Supine Systolic Blood Pressure (mmHg)	Supine Diastolic Blood Pressure (mmHg)	Pulse Oximetry (%)	Body Temperature (°C)

Listing 16.2.8.6
Vital Signs Change from Baseline

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Supine Heart Rate (beats/min)	Supine Systolic Blood Pressure (mmHg)	Supine Diastolic Blood Pressure (mmHg)

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

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Listing 16.2.8.7
Vital Signs Overall Qualitative Results Abnormal Assessments

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Collection Date	Collection Time	Assessment	Interpretation
						ABNORMAL, NCS
						ABNORMAL, CS

NCS = Not Clinically Significant, CS = Clinically Significant

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Listing 16.2.8.8
12 Lead ECG Quantitative Findings

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Timepoint	Collection Date	Collection Time	Heart Rate (beats/min)	PR (msec)	RR (msec)	QRS (msec)	QT (msec)	QTcB (msec)	QTcF (msec)

QTcB = QT corrected according to Bazett, QTcF = QT corrected according to Fridericia.

Listing 16.2.8.9
12 Lead ECG Change From Baseline

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Timepoint	Collection Date	Collection Time	QT (msec)	QTcB (msec)	QTcF (msec)

Baseline is defined as: Visit 2 in the MIV-711-201 for Group A, Visit 8 in the MIV-711-201 for Group B

QTcB = QT corrected according to Bazett, QTcF = QT corrected according to Fridericia.

Listing 16.2.8.10
12 Lead ECG Overall Qualitative Assessment

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Timepoint	Collection Date	Collection Time	Assess-ment	Interpretation	Comment

NCS = Not Clinically Significant, CS = Clinically Significant

Listing 16.2.8.11
Physical Examination Abnormal Findings

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Exam Date	Exam Time	Body System	Abnormality	Clinical Significance NCS	Clinical Significance CS

NCS = Not Clinically Significant, CS = Clinically Significant

Listing 16.2.8.12
Patient Weight

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Date	Time	Weight (kg)

Listing 16.2.8.13
Phone Call to Assess Safety

Study Group = Group A

Patient MIV-711-202	Patient MIV-711-201	Visit	Comments