Figure 1. DISKO Trial CONSORT Flowchart

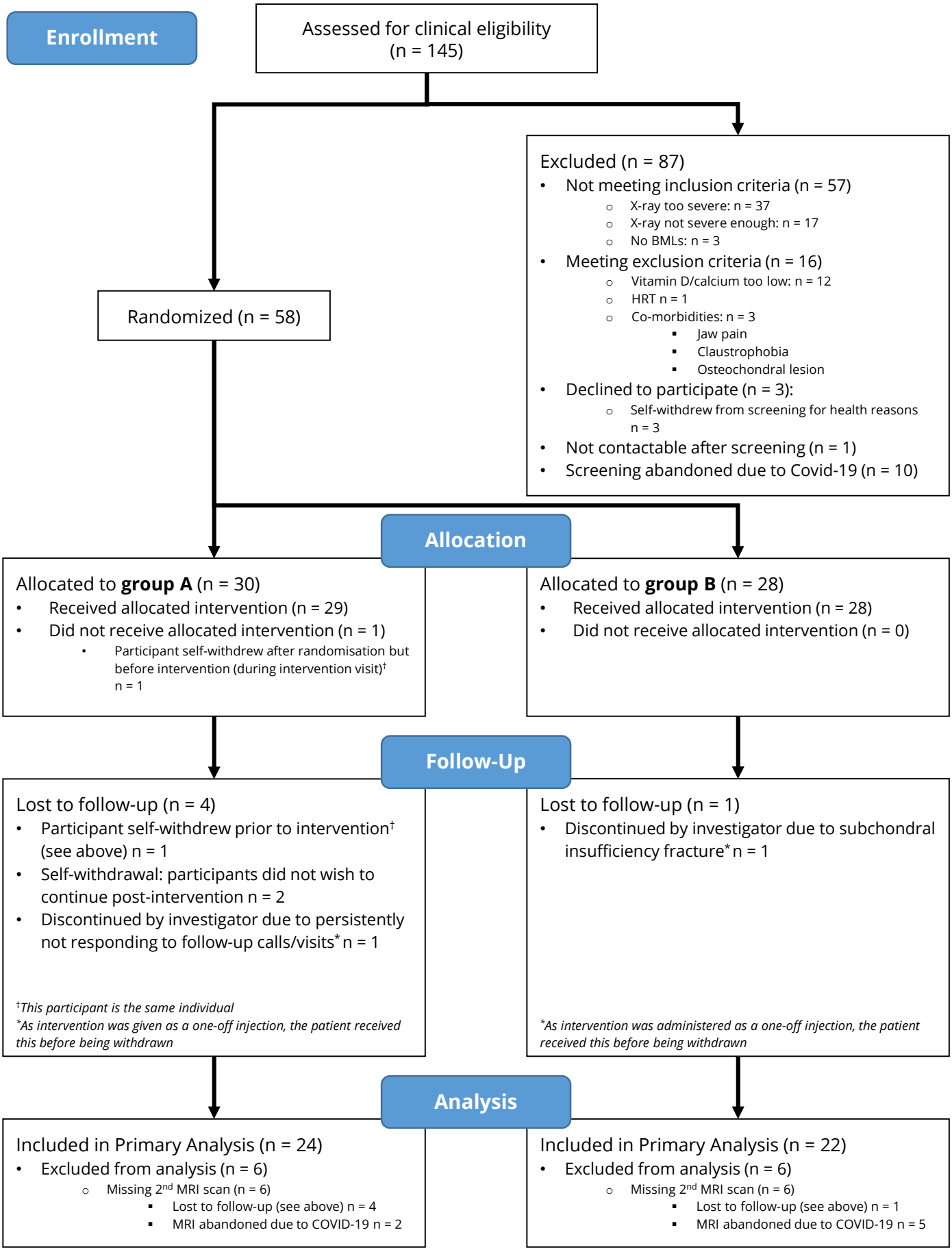

Table 1. Baseline Characteristics of Study Sample

Outcome, units/range		Group A (total N = 30)		Group B (total N = 28)		TOTAL (total N = 58)	
		Obs	Statistic	Obs	Statistic	Obs	Statistic
	format	*N*		*N*		*N*	
Age at screening visit, years	mean (SD)	30	65.33 (7.57)	28	62.89 (7.70)	58	64.16 (7.67)
BMI at screening visit, kg/m^2	mean (SD)	30	29.47 (4.81)	28	29.12 (4.64)	58	29.30 (4.69)
Initial Vitamin D level, nmol/l	median (IQR)	30	53.50 (42.80 to 73.80)	28	51.15 (42.45 to 63.35)	58	52.80 (42.80 to 67.60)
Post-supplemental Vitamin D level (if applicable), nmol/l	median (IQR)	11	73.70 (61.00 to 87.20)	11	69.30 (60.90 to 78.70)	22	71.35 (61.00 to 78.70)
Vitamin D level at study start*, nmol/l	median (IQR)	30	67.35 (57.40 to 77.20)	28	64.10 (54.35 to 77.05)	58	66.55 (56.90 to 77.20)
HADS Anxiety Subscale score at baseline visit, 0 to 21	mean (SD)	29	5.34 (3.60)	28	4.18 (2.82)	57	4.77 (3.27)
HADS Depression Subscale score at baseline visit, 0 to 21	mean (SD)	29	4.41 (3.13)	28	3.32 (2.79)	57	3.88 (2.99)
SF-12 Physical Composite Aggregate at baseline visit, 0 to 100	mean (SD)	29	52.33 (9.42)	27	58.11 (8.19)	56	55.12 (9.24)
SF-12 Mental Composite Aggregate at baseline visit, 0 to 100	mean (SD)	29	40.39 (8.96)	27	39.34 (8.49)	56	39.88 (8.68)
IPQ-B Score at baseline visit, 0 to 80	mean (SD)	29	13.90 (10.50)	27	12.07 (9.14)	56	13.02 (9.82)
EQ-5D-5L Index Score, -0.13 to 1**	mean (SD)	30	0.60 (0.20)	27	0.66 (0.11)	57	0.63 (0.16)
EQ-5D-5L Overall Health Status VAS, 0 to 100	mean (SD)	29	77.24 (14.30)	27	80.30 (13.88)	56	78.71 (14.06)
EQ-5D-5L Pain & Discomfort Subscale, 1 to 5	mean (SD)	30	2.43 (0.90)	27	2.37 (0.74)	57	2.40 (0.82)
EQ-5D-5L Usual Activities Subscale, 1 to 5	mean (SD)	30	1.40 (0.72)	27	1.19 (0.40)	57	1.30 (0.60)
EQ-5D-5L Mobility Subscale, 1 to 5	mean (SD)	30	2.37 (0.96)	27	2.11 (0.70)	57	2.25 (0.85)
EQ-5D-5L Self Care Subscale, 1 to 5	mean (SD)	30	2.90 (0.80)	27	2.89 (0.64)	57	2.89 (0.72)
EQ-5D-5L Anxiety/Depression Subscale, 1 to 5	mean (SD)	30	1.60 (0.77)	27	1.11 (0.42)	57	1.37 (0.67)
Pain in the last week NRS, 0 to 10	mean (SD)	30	5.93 (1.72)	27	6.15 (1.77)	57	6.04 (1.73)
Pain on nominated activity NRS, 0 to 10	mean (SD)	23	6.83 (1.64)	26	6.77 (1.70)	49	6.80 (1.66)
KOOS Pain Subscale, 100 to 0	mean (SD)	30	51.57 (14.96)	28	54.76 (17.52)	58	53.11 (16.18)
KOOS Symptom Subscale, 100 to 0	mean (SD)	30	45.83 (10.06)	28	41.96 (12.36)	58	43.97 (11.30)
KOOS Activities of Daily Living Subscale, 100 to 0	mean (SD)	29	53.80 (16.16)	28	60.29 (15.83)	57	56.99 (16.19)
KOOS Sport & Recreation Subscale, 100 to 0	mean (SD)	30	25.33 (21.37)	27	36.30 (23.39)	57	30.53 (22.83)
KOOS Quality of Life Subscale, 100 to 0	mean (SD)	30	34.58 (15.55)	28	37.05 (16.92)	58	35.78 (16.13)
WOMAC Pain Subscale, 100 to 0	mean (SD)	30	55.67 (18.18)	28	59.46 (20.25)	58	57.50 (19.13)
WOMAC Function Subscale, 100 to 0	mean (SD)	29	53.80 (16.16)	28	60.29 (15.83)	57	56.99 (16.19)
WOMAC Stiffness Subscale, 100 to 0	mean (SD)	30	46.25 (17.10)	28	46.43 (21.75)	58	46.34 (19.31)
BML Area, mm^2	median (IQR)	30	701.50 (312.00 to 1093.00)	28	876.00 (543.00 to 1368.00)	58	787.50 (370.00 to 1150.00)
BML Volume, mm^3	median (IQR)	30	5157.00 (2150.00 to 9342.00)	28	6667.00 (4142.50 to 9623.00)	58	6109.50 (2468.00 to 9342.00)
Synovitis volume (tissue and fluid combined), mm^3	median (IQR)	30	9183.37 (6038.96 to 14805.53)	28	6760.32 (4555.09 to 11611.83)	58	8520.62 (5157.15 to 13827.34)

Obs = Number of Observations; BMI = Body Mass Index; HADS = Hospital Anxiety and Depression Scale; IPQ-B = Brief Illness Perception Questionnaire; BML = Bone Marrow Lesion; NRS = Numerical Rating Scale; KOOS = Knee Osteoarthritis Outcome Score; WOMAC = Western Ontario and McMaster Universities Arthritis Index

**At study start = either vitamin D level at initial test if sufficient, or post-supplementation if initially insufficient. 11 participants received supplementation prior to study start due to initial insufficiency.*

***EQ-5D-5L Index Score is calibrated against population norms, hence the unusual scale units. In the DISKO trial sample, index scores ranged from -0.13 to 1.00.*

List of Outcomes Collected in the DISKO Trial

Primary Outcome

- Total bone marrow lesion (BML) area (mm^2), at 6 months.

Secondary Outcomes

- Overall perceived knee pain/discomfort in the last week, 0-10 numerical rating scale ($NRS_{last\ week}$), at 3 and 6 months.
- Knee pain on nominated aggravating activity, 0-10 numerical rating scale (NRS_{NA}), at 3 and 6 months.
- Knee Osteoarthritis Outcome Score (KOOS), at 3 and 6 months. This includes all 5 subscales of the
- KOOS questionnaire subscales (score 100 – 0)
    - Pain
    - Symptoms
    - Activities of Daily Living
    - Sport and Recreation
    - Quality of Life
        - The WOMAC Pain, Stiffness and Function Subscales can be derived from these scores also.
- EuroQol five dimensions questionnaire (EQ-5D-5L), at 3 and 6 months. This includes all subscales:
    - Overall Index Score
    - Overall Health Status Visual Analogue Scale
    - Pain and Discomfort
    - Usual Activities
    - Mobility
    - Self Care
    - Anxiety/Depression
- 12-Item Short Form Health Survey (SF-12), at 3 and 6 months:
    - Mental aggregate score (unnormalised).
    - Physical aggregate score (unnormalised)
- Total bone marrow lesion (BML) volume (mm^3), at 6 months.
- Total synovitis (both synovial tissue and fluid, combined) volume (mm^3), at 6 months.
- Adverse event rate (AEs), at 3 and 6 months.

Adverse Event Data

Note: 2 adverse events occurred in the screening period of the DISKO trial, prior to randomisation.

Table 2. Severity Grading of Adverse Events, by Group Allocation

Adverse Event Severity Rating	Group A	Group B	Pre-randomisation	Total
	N	*N*	*N*	*N*
Mild	22	16	2	40
Moderate	7	11	0	18
Severe	1	0	0	1
Total	30	27	2	59

Table 3. Breakdown of Adverse Event Categories, by Group Allocation

Adverse Event Category	Group A	Group B	Pre-randomisation	Total
	N	*N*	*N*	*N*
Musculoskeletal	11	10	2	23
Cardiovascular	4	1	0	5
Gastrointestinal	2	3	0	5
Respiratory	1	4	0	5
Dermatological	3	0	0	3
Laboratory Abnormality	1	2	0	3
Urinary	2	1	0	3
General (Non-specific)	2	0	0	2
Viral Illness	1	1	0	2
Ear & Labyrinth Disorders, Other	0	1	0	1
Fatigue	1	0	0	1
Gastrointestinal Disorder, Other	0	1	0	1
Limb Trauma	1	0	0	1
Minor Surgery	0	1	0	1
Respiratory, Thoracic, and Mediastinal Disorders - Other	1	0	0	1
Trauma - Head	0	1	0	1
Trauma - Non-specified	0	1	0	1
Total	30	27	2	59

Table 4. Number of, and Average, Adverse Events per Trial Participant

Number of Adverse Events Per Participant	Frequency
1 Adverse Event	19
2 Adverse Events	8
3 Adverse Events	5
4 Adverse Events	1
5 Adverse Events	1
Mean Adverse Events Per Participant	1.74
Total Adverse Events	59

Table 5. Participants Experiencing One or More Adverse Events At or After Intervention, by Intervention Group

Participants Experiencing One or More Adverse Events	Group A	Group B	Total
	N	*N*	*N*
No Adverse Events	14	12	26
1 or More	16	16	32
Total	30	28	58

Test for differences in event rate between groups: $\chi^2 = 0.085$; $p = 0.77$

Note: Two additional participants experienced adverse events during the approximately 2-week screening period prior to randomisation.

Table 6. Details of All Serious Adverse Events in the DISKO Trial

SAE Description	Date Randomised (Date of Intervention)	Onset Date	Outcome	Resolved Date	Days Since Intervention	Days from Onset Until Resolved	Grade	Hospital Admission?	Fatal?	Caused a Disability?	Life Threatening?	Related to Any Study Intervention?*	Expected?
Haematuria	29-Mar-19	02-Oct-19	Resolved	06-Oct-19	187	4	2	Yes	No	No	No	No	N/A
Asthma Attack	26-Feb-20	06-Jan-20	Resolved	11-Jan-20	-51[†]	5	3	Yes	No	No	No	No	N/A

[*]Related to treatment or MRI procedure or supplementation

[†]Participant experienced an SAE 51 days prior to receiving trial intervention (i.e. during screening period, prior to randomisation)