Supplementary Materials

Efficacy and safety of fasinumab in patients with chronic low back pain: a phase II/III randomized clinical trial

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Supplementary Methods

Inclusion criteria

A patient must have met all of the following criteria to be eligible for inclusion in the study:

1. Male or female ≥35 years of age at the screening visit
2. Provided signed informed consent
3. Body mass index ≤39 kg/m^2
4. Clinical diagnosis of chronic moderate-to-severe LBP for ≥3 months (prior to the screening visit)
    a. Quebec taskforce category 1 (pain without radiation) or category 2 (pain with proximal radiation above the knee)
    b. Primary pain location between 12th thoracic vertebra and lower gluteal fold
    c. At both the screening and the randomization visit, an LBPI NRS score of ≥4 over the previous 24 hours
    d. During the pre-randomization period, mean daily LBPI score of ≥4
    e. At the screening visit, PGA of LBP of fair, poor, or very poor
5. History of regular analgesic medication, such as NSAIDs, COX-2 inhibitors, opioids, paracetamol/acetaminophen, or a combination thereof
    a. Taking medication >4 days per week in the month prior to screening

   b. Willing to discontinue current opioid pain medications starting at pre-randomization visit through the week 16 study visit

   c. Willing to discontinue current NSAID pain medications (oral or topical) starting at pre-randomization visit through 16 weeks after last dose of study drug

6. A history of inadequate pain relief or intolerance to analgesics used for chronic LBP as defined by:

   a. Intolerance or inadequate pain relief from paracetamol/acetaminophen, and

   b. Intolerance or inadequate pain relief from at least 1 oral NSAID, and

   c. Intolerance or inadequate pain relief from at least 1 opioid, unwillingness to take opioid therapy, or lack of access to opioid therapy

7. Willing to consider TJR surgery, if necessary
   NOTE: This inclusion criterion was added in protocol amendment 2

8. Willing and able to comply with clinic visits and study-related procedures

9. Able to understand and complete study-related questionnaires

Exclusion criteria

A patient who met any of the following criteria was excluded from the study:

1. Four or more consecutive LBPI NRS data entries missed during the pre-randomization period.

2. History of Quebec taskforce category >2 (pain with proximal radiation above the knee) lumbosacral radiculopathy within the past 2 years prior to the screening visit

3. Patient was not a candidate for MRI

4. Evidence on baseline lumbar spine MRI (or lumbar spine X-ray, if requested) of severe spinal stenosis, disc herniation with substantial neural encroachment, recent vertebral fracture, an active destructive process, or marked segmental instability (as indicated by bone marrow oedema or Modic type I change, respectively)

5. History of major trauma, or back surgery in the past 6 months prior to the screening visit.

6. History or presence of pyriformis syndrome

7. History or presence at the screening visit of non-OA inflammatory joint disease (e.g. rheumatoid arthritis, lupus erythematosus, psoriatic arthritis, pseudogout, joint infections), multiple sclerosis, seronegative spondyloarthropathy, Paget's disease of the spine, pelvis, or femur, fibromyalgia, or tumours or infections of the spinal cord

8. Use of extended-release opioids or long-acting opioids such as oxycodone controlled-release, oxymorphone extended release, hydromorphone, transdermal fentanyl, or methadone within 3 months prior to the screening visit

9. Use of a monoamine reuptake inhibitor, tricyclic antidepressants, selective serotonin reuptake inhibitors, and serotonin norepinephrine reuptake inhibitors for treatment of pain within 4 weeks prior to the screening visit
10. Systemic (i.e. oral or intramuscular) corticosteroids or intra-articular corticosteroid injections within 30 days prior to the screening visit
11. Epidural steroid injections within 3 months prior to the screening visit
12. Botox injections for LBP within 6 months prior to the screening visit
13. History or presence on imaging of arthropathy (osteonecrosis, subchondral insufficiency fracture, rapidly progressing OA type 1 or type 2), stress or recent fracture, neuropathic joint arthropathy, hip dislocation (prosthetic hip dislocation is eligible), knee dislocation (patella dislocation is eligible), congenital hip dysplasia with degenerative joint disease, extensive subchondral cysts, evidence of bone fragmentation or collapse, or primary metastatic tumour with the exception of chondromas or pathological fractures during the screening period
14. Was scheduled for a joint replacement surgery during the study period
15. Signs and symptoms of carpal tunnel syndrome within 6 months of screening
16. History or presence at the screening visit of autonomic neuropathy, diabetic neuropathy, or other peripheral neuropathy including reflex sympathetic dystrophy
17. Evidence of autonomic neuropathy at the screening visit, as defined in the Survey of Autonomic Symptoms

18. History or diagnosis of chronic autonomic failure syndrome including pure autonomic failure and multiple system atrophy (Shy-Drager syndrome)

19. Poorly controlled diabetes (Haemoglobin A1c [HbA1c] >9.0%) at the screening visit

20. Confirmed elevated screening alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >2.5x upper limit of normal (ULN)
    NOTE: This inclusion criterion was added in protocol amendment 1

21. Resting heart rate of <50 beats per minute (bpm) at the screening, pre-randomization, or randomization visits

22. History or presence of 2nd or 3rd degree heart block, 1st degree heart block with abnormal QRS, or bifascicular block by ECG at the screening visit

23. History or presence of orthostatic hypotension at the screening, pre-randomization, or baseline visits

24. Poorly controlled hypertension

    - Systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg at the screening visit

    - Systolic blood pressure of 160 mm Hg to 179 mm Hg or diastolic blood pressure of 100 mm Hg to 109 mm Hg at the screening visit, AND a history of end-organ damage (including history of left ventricular hypertrophy, heart failure, angina, myocardial infarction, stroke, transient ischemic attack (TIA), peripheral arterial disease, and moderate to advanced retinopathy [haemorrhages or exudates, papilledema])

25. Congestive heart failure with NY Heart Classification of stage 3 or 4

26. TIA or cerebrovascular accident within the past 12 months prior to the screening visit, or myocardial infarction or acute coronary syndromes within the past 6 months prior to the screening visit

27. Significant concomitant illness including, but not limited to, psychiatric, cardiac, renal, hepatic, neurological, endocrinological, metabolic, or lymphatic disease that, in the opinion of the investigator, would adversely affect the patient's participation in the study

28. New major illness diagnosed within 2 months prior to the screening visit

29. Known history of ocular herpes simplex virus, herpes simplex virus pneumonia, or herpes simplex virus encephalitis

30. Known history of human immunodeficiency virus infection

31. Known history of infection with hepatitis B virus. Patients with a history of hepatitis B are eligible if there is documentation of a negative test for hepatitis B surface antigen and a positive test for antibodies to the hepatitis B virus surface antigen

32. Known history of infection with hepatitis C virus. Patients with a history of hepatitis C are eligible if there is documentation of a negative hepatitis C virus RNA test

33. History or presence of malignancy within the last 5 years prior to screening, except patients who have been treated successfully with no recurrence for >1

year of basal cell or squamous cell carcinoma of the skin or in-situ cervical cancer

34. Known allergy or sensitivity to doxycycline or related compounds, or monoclonal antibodies

35. History of (within 5 years prior to the screening visit) current alcoholism, alcohol abuse, substance abuse, or abuse of prescription pain medication

36. History of cannabis use for the treatment of pain within the past 6 months prior to the screening visit

37. History of hospital admission for depression or suicide attempt within 5 years or active, severe major depression at screening

38. Current or pending worker's compensation, litigation, disability, or any other monetary settlement related to LBP

39. Ongoing participation in a clinical research study evaluating another investigational drug or having received another investigational product within 30 days or 5 half-lives, whichever is longer

40. Exposure to an anti-NGF antibody within 6 months prior to the screening visit or known sensitivity or intolerance to anti-NGF antibodies

41. Pregnant or breast-feeding women

42. Women of childbearing potential who had a positive pregnancy test result or did not have their pregnancy test result at baseline

43. Women of childbearing potential who were unwilling to use acceptable contraceptive methods during the study and for 20 weeks after the last dose of study drug. Acceptable methods of contraception included combined (oestrogen and progesterone containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal); progesterone-only hormonal contraception associated with inhibition of ovulation (oral, injectable, or implantable); intrauterine device; intra-uterine hormone-releasing system; bilateral tubal occlusion; vasectomized partner; sexual abstinence; or condom in combination with either cap, diaphragm, or sponge with spermicide (double-barrier contraception).

Safety monitoring

An independent data monitoring committee (DMC), consisting of statistical and medical experts, met periodically to review unblinded data as the study progressed. The DMC assessed the safety of fasinumab, with a focus on joint-related adverse events, sympathetic nervous system dysfunction, and neurosensory disturbances. The DMC made recommendations to the sponsor based on the conduct of the study, however no action was requested during the study period.

An independent blinded adjudication committee composed of musculoskeletal radiologists reviewed images for joint AEs, pre-operative images in patients undergoing joint replacements, and routine study scheduled images of suspicious findings by the central reader, for AAs. Positive adjudications met the definition for one or more of the following categories: rapidly progressive osteoarthritis (RPOA) type 1 (RPOA1), RPOA type 2 (RPOA2), subchondral insufficiency fracture (SIF), or primary osteonecrosis. RPOA1 was defined as joint space narrowing exceeding pre-

specified thresholds. For knee joints with a baseline joint space width (JSW) ≥2 mm, reduction had to be ≥2 mm or 50% from baseline at any time point during the study, whichever was greater. For knee joints with baseline JSW <2 mm, a reduction of JSW to 0 mm qualified as RPOA1. For hip joints; if JSW was >1.5 mm at baseline, a reduction of >1.5 mm from baseline qualified as RPOA1. If JSW was <1.5 mm at baseline, then a reduction in JSW to 0 mm also qualified as RPOA1. RPOA2 was defined as changes in bone structure on plain film or magnetic resonance imaging (MRI), atypical of advanced OA. Subchondral insufficiency fracture was defined as subchondral radiolucency, which could have a possible sclerotic linear component and articular surface flattening, confirmed by MRI. Primary osteonecrosis was defined as a focal circumscribed or extended region of mottled radiolucency without evidence of subchondral collapse or bone fragmentation, confirmed by MRI. Because the categories are not always considered mutually exclusive, particularly when reviewing MRIs, the adjudication process across the fasinumab program was updated during the conduct of the study such that the adjudication committee had the option to select more than one category simultaneously in a single joint. All patients received x-rays of the knees, hips, and shoulders at screening as well as MRI of any knee or hip with K-L score ≥3.

Analysis sets

The safety analysis set included all randomized patients who received any study drug. The full analysis set included all randomized patients and was based on the treatment allocated (as randomized). The full analysis set was used to perform sensitivity analysis for the primary and selected secondary endpoints.

A modified intent-to-treat set (mITT) was specified in the final SAP, before database lock, in response to the unplanned early termination of dosing in the study. This set included all randomized patients who received at least one dose of study drug based on the treatment allocated (as randomized) including data up to 5 weeks after the last dose of study drug. Originally, the efficacy data in the study was to be analyzed based on data collected up to week 16, which was 4 weeks after the last planned dose of study therapy for patients receiving fasinumab Q4W. However, with the early cessation of dosing, many patients at week 16 would have discontinued dosing more than 5 weeks before the week 16 visit and thus would not be expected to continue to derive efficacy from the study drug. Thus, this modification to the treatment set was implemented.

Statistical analysis

The primary efficacy endpoint, change from baseline to week 16 in LBPI NRS score, was analysed using a mixed-effect model repeated measures approach based on the mITT analysis set. The model included the randomization strata, baseline LBPI score, treatment, study week, and treatment-by-week interaction. Denominator degrees of freedom were estimated using Kenward-Roger's approximation. Data from all patients, including data collected after discontinuing treatment up to the earlier of withdrawal of consent, week 16, or 5 weeks after the last dose of study drug, were used in the primary efficacy analyses according to the intent-to-treat principle using the MMRM approach with no imputation for missing data. Additional sensitivity analysis was performed using the full analysis set, which included all randomized patients, for the primary and secondary endpoints.

Supplementary Results

Patient disposition

Approximately 30% (166 patients) of the 563 randomized patients completed the week 16 end of treatment visit before the study was placed on partial clinical hold. Of these patients, six discontinued treatment early due to an AE (three patients), physician decision (two patients), or withdrawal by patient (one patient). The remaining 70% (397 patients) did not complete dosing through the end of the treatment period (week 16 visit) before the study was placed on partial clinical hold. Across the treatment groups, 42% to 54% of these patients were followed for safety and completed their remaining visits to week 36 following the partial clinical hold.

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Supplementary Table 1. Study drug administration (safety analysis set)

		Fasinumab			
	Placebo (n=140)	**6 mg SC Q4W (n=139)**	**9 mg SC Q4W (n=139)**	**9 mg IV Q8W (n=140)**	**Total (N=558)**
SC study drug injection*					
Compliance (%), mean (SD)	94.3 (15.0)	95.1 (14.1)	97.5 (11.6)	95.0 (14.4)	95.5 (13.9)
Number of SC injections (% of patients)					
1	33 (23.6%)	32 (23.0%)	33 (23.7%)	34 (24.3%)	132 (23.7%)
2	33 (23.6%)	32 (23.0%)	28 (20.1%)	28 (20.0%)	121 (21.7%)
3	23 (16.4%)	26 (18.7%)	19 (13.7%)	22 (15.7%)	90 (16.1%)
4	51 (36.4%)	49 (35.3%)	59 (42.4%)	56 (40.0%)	215 (38.5%)
IV study drug infusion					
Compliance (%), mean (SD)	95.7 (14.1)	95.3 (15.8)	98.9 (7.3)	97.5 (10.9)	96.9 (12.5)
Number of IV injections (% of patients)					
1	68 (48.6%)	67 (48.2%)	61 (43.9%)	64 (45.7%)	260 (46.6%)
2	72 (51.4%)	71 (51.1%)	78 (56.1%)	76 (54.3%)	297 (53.2%)
Missing	0	1	0	0	1
Mean total fasinumab dose/patient, mg	N/A	22.0	33.7	13.9	N/A

*SC treatment included loading dose as well as nominal dose on day of first study drug treatment

Compliance = (Number of actual injections or infusions of study drug during exposure period)/(Number of planned injections or infusions of study drug during exposure period on or before the time that the patient discontinued from the study) x 100%.

IV, intravenous; N/A, not applicable; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; SD, standard deviation.

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Supplementary Table 2. Change from baseline to week 16 in the average daily LBPI NRS, RMDQ, and PGA of LBP scores in patients with and without OA of the peripheral joints (mITT analysis set)

		Fasinumab		
	Placebo	**6 mg SC Q4W**	**9 mg SC Q4W**	**9 mg IV Q8W**
		LBPI NRS		
Patients with OA of the peripheral joints, n	82	92	68	78
Baseline average daily LBPI NRS score, mean (SD); n	6.4 (1.2); 81	6.6 (1.3); 90	6.7 (1.4); 68	6.2 (1.1); 78
Week 8				
Average daily LBPI NRS score, mean (SD); n	5.6 (2.1); 55	4.8 (2.1); 62	3.9 (2.3); 51	4.0 (2.2); 59
Change from baseline to week 8, mean (SD); n	–1.0 (2.0)	–1.9 (2.1)	–2.7 (1.9)	–2.2 (2.0)
LS mean (SE)	–0.9 (0.3)	–1.8 (0.2)	–2.6 (0.3)	–2.2 (0.3)
95% CI	(–1.39, –0.40)	(–2.24, –1.31)	(–3.11, –2.08)	(–2.67, –1.70)
Difference vs placebo, LS mean (SE)		–0.9 (0.3)	–1.7 (0.4)	–1.3 (0.3)
95% CI		(–1.53, –0.22)	(–2.40, –1.00)	(–1.96, –0.62)
Week 16				
Average daily LBPI NRS score, mean (SD); n	4.5 (2.4); 32	4.2 (2.1); 32	3.6 (2.2); 26	4.0 (2.5); 34
Change from baseline to week 16, mean (SD); n	–2.1 (2.4); 31	–2.5 (2.0); 32	– 2.9 (1.8); 26	–2.2 (2.0); 34
LS mean (SE)	–1.7 (0.3)	–2.0 (0.3)	–2.6 (0.3)	–2.3 (0.3)
95% CI	(–2.26, –1.09)	(–2. 56, –1.43)	(–3.20, –1.94)	(–2.84, –1.70)

Difference vs placebo, LS mean (SE)		–0.3 (0.4)	–0.9 (0.4)	–0.6 (0.4)
95% CI		(–1.11, 0.48)	(–1.73, –0.04)	(–1.39, 0.21)
Patients without OA of the peripheral joints, n	58	47	71	62
Baseline average daily LBPI NRS score, mean (SD); n	6.6 (1.4); 58	6.3 (1.3); 47	6.7 (1.2); 71	6.7 (1.2); 62
Week 8				
Average daily LBPI NRS score, mean (SD); n	4.9 (2.0); 41	4.5 (1.7); 37	4.6 (2.5); 54	4.3 (2.6); 44
Change from baseline to week 8, mean (SD); n	–1.7 (1.4); 41	–1.8 (1.5); 37	–2.1 (2.4); 54	–2.3 (2.6); 44
LS mean (SE)	–1.6 (0.3)	–1.6 (0.4)	–1.9 (0.3)	–2.2 (0.3)
95% CI	(–2.26, –0.94)	(–2.37, –0.90)	(–2.58, –1.26)	(–2.82, –1.49)
Difference vs placebo, LS mean (SE)		–0.0 (0.4)	–0.3 (0.4)	–0.6 (0.40)
95% CI		(–0.87, 0.80)	(–1.08, 0.44)	(–1.34, 0.23)
Week 16				
Average daily LBPI NRS score, mean (SD); n	4.9 (1.2); 18	4.6 (1.4); 16	4.7 (2.2); 29	3.8 (2.4); 22
Change from baseline to week 16, mean (SD); n	–1.4 (1.5); 18	–1.5 (1.5); 16	–2.4 (2.1); 29	–2.9 (2.5); 22
LS mean (SE)	–1.7 (0.4)	–1.9 (0.4)	–2.2 (0.4)	–2.6 (0.4)
95% CI	(–2.47, –1.01)	(–2.66, –1.06)	(–2.91, –1.53)	(–3.29, –1.84)
Difference vs placebo, LS mean (SE)		–0.1 (0.5)	–0.5 (0.4)	–0.8 (0.5)
95% CI		(–1.08, 0.84)	(–1.34, 0.38)	(–1.73, 0.07)

RMDQ

Patients with OA of the peripheral joints, n	82	92	68	78
Baseline RMDQ total score, mean (SD); n	11.1 (4.8); 74	11.4 (5.1); 90	10.3 (5.0); 67	11.7 (5.4); 75
Week 8				
RMDQ total score, mean (SD); n	8.7 (5.5); 58	6.2 (5.4); 63	4.8 (4.9); 51	5.5 (5.0); 60
Change from baseline to week 8, mean (SD); n	–2.6 (4.1); 50	–5.5 (5.7); 61	–5.3 (5.1): 50	–7.0 (5.4); 57
LS mean (SE)	–2.4 (0.6)	–5.1 (0.5)	–6.0 (0.6)	–6.1 (0.6)
95% CI	(–3.60, –1.27)	(–6.16, –4.05)	(–7.22, –4.85)	(–7.27, –5.02)
Difference vs placebo, LS mean (SE)		–2.7 (0.8)	–3.6 (0.8)	–3.7 (0.8)
95% CI		(–4.19, –1.15)	(–5.23, –1.98)	(–5.28, –2.14)
Week 16				
RMDQ total score, mean (SD); n	6.5 (5.8); 32	4.6 (4.4); 33	3.5 (3.0); 26	4.9 (4.9); 34
Change from baseline to week 16, mean (SD); n	–3.9 (4.5); 28	–7.2 (6.0); 31	–6.8 (4.5); 26	–6.6 (5.7); 32
LS mean (SE)	–3.3 (0.7)	-6.4 (0.6)	–6.6 (0.7)	–6.5 (0.7)
95% CI	(–4.64, –1.92)	(–7.69, –5.16)	(–7.99, –5.19)	(–7.82, –5.23)
Difference vs placebo, LS mean (SE)		–3.1 (0.9)	–3.3 (1.0)	–3.2 (0.9)
95% CI		(–4.96, –1.33)	(–5.24, –1.39)	(–5.08, –1.42)
Patients without OA of the peripheral joints	58	47	71	62
Baseline RMDQ total score, mean (SD); n	10.6 (5.9); 58	9.7 (5.1); 45	11.1 (6.3); 69	11.6 (5.1); 61
Week 8				
RMDQ total score, mean (SD); n	6.7 (5.6); 42	5.0 (4.8); 38	6.9 (6.1); 54	5. 9 (6.0); 44

Change from baseline to week 8, mean (SD); n	–3.8 (5.6); 42	–5.2 (4.6); 36	–4.2 (4.6); 52	–5.1 (5.3)
LS mean (SE)	–4.5 (0.8)	–6.3 (0.9)	–5.0 (0.7)	–6.4 (0.8)
95% CI	(–6.04, –3.05)	(–8.02, –4.62)	(–6.57, –3.52)	(–7.90, –4.83)
Difference vs placebo, LS mean (SE)		–1.8 (1.0)	–0.5 (0.9)	–1.8 (0.9)
95% CI		(–3.69, 0.13)	(–2.23, 1.23)	(–3.61, –0.04)
Week 16				
RMDQ total score, mean (SD); n	6.7 (5.4); 18	6.2 (5.9); 15	6.0 (5.4); 29	5.2 (5.9); 23
Change from baseline to week 16, mean (SD); n	–3.7 (4.6); 18	–3.7 (4.4); 15	–5.7 (5.0); 29	–6.7 (5.6); 23
LS mean (SE)	–5.1 (0.9)	–5.8 (1.0)	–6.1 (0.8)	–6.7 (0.9)
95% CI	(–6.82, –3.37)	(–7.74, –3.85)	(–7.71, –4.44)	(–8.38, –4.98)
Difference vs placebo, LS mean (SE)		–0.7 (1.2)	–1.0 (1.0)	–1.6 (1.1)
95% CI		(–3.02, 1.63)	(–3.03, 1.07)	(–3.71, 0.54)
		PGA of LBP		
Patients with OA of the peripheral joints, n	82	92	68	78
Baseline PGA, mean (SD); n	3.5 (0.7); 82	3.5 (0.7); 92	3.3 (0.9); 68	3.4 (0.6); 78
Week 8				
PGA, mean (SD); n	3.1 (0.8); 58	2.7 (0.9); 63	2.4 (0.9); 51	2.6 (0.9); 60
Change from baseline to week 8, mean (SD); n	–0.5 (0.8); 58	–0.8 (1.0); 63	–0.9 (1.1); 51	–0.9 (0.9); 60
LS mean (SE)	–0.5 (0.1)	–0.8 (0.1)	–1.0 (0.1)	–0.8 (0.1)
95% CI	(–0.67, –0.25)	(–1.00, –0.60)	(–1.19, –0.74)	(–1.05, –0.63)
Difference vs placebo, LS mean (SE)		–0.3 (0.1)	–0.5 (0.2)	–0.4 (0.2)

95% CI		(–0.61, –0.05)	(–0.80, –0.20)	(–0.66, –0.08)
Week 16				
PGA, mean (SD); n	2.7 (0.8); 32	2.4 (0.9); 33	2.3 (0.9); 26	2.3 (1.0); 34
LS mean (SE)	–0.7 (0.1)	–0.9 (0.1)	–1.0 (0.2)	–1.0 (0.1)
95% CI	(–0.98, –0.45)	(–1.16, –0.64)	(–1.26, –0.68)	(–1.25, –0.73)
Difference vs placebo, LS mean (SE)		–0.2 (0.2)	–0.3 (0.2)	–0.3 (0.2)
95% CI		(–0.55, 0.18)	(–0.65, 0.13)	(–-0.64, 0.09)
Patients without OA of the peripheral joints, n	58	47	71	62
Baseline PGA, mean (SD); n	3.6 (0.7); 58	3.4 (0.7); 47	3.4 (0.7); 71	3.4 (0.8); 62
Week 8				
PGA, mean (SD); n	3.0 (0.7); 42	2.7 (0.8); 38	2.7 (0.9); 54	2.5 (1.1); 44
Change from baseline to week 8, mean (SD); n	–0.6 (0.9); 42	–0.8 (0.8); 38	–0.7 (0.8); 54	–0.9 (1.0); 44
LS mean (SE)	–0.6 (0.1)	–0.8 (0.2)	–0.7 (0.1)	–1.0 (0.1)
95% CI	(–0.84, –0.31)	(–1.08, –0.50)	(–0.97, –0.44)	(–1.28, –0.74)
Difference vs placebo, LS mean (SE)		–0.2 (0.2)	–0.1 (0.2)	–0.4 (0.2)
95% CI		(–0.55, 0.13)	(–0.43, 0.19)	(–0.76, –0.12)
Week 16				
PGA, mean (SD); n	3.0 (0.6); 18	2.7 (1.0); 15	2.7 (1.0); 29	2.4 (0.9); 23
Change from baseline to week 16, mean (SD); n	–0.6 (0.6); 18	–0.5 (1.1); 15	–0.8 (0.8); 29	–1.0 (0.9); 23
LS mean (SE)	–0.7 (0.2)	–0.9 (0.2)	–0.8 (0.1)	–1.1 (0.2)
95% CI	(–0.99, –0.39)	(–1.20, –0.54)	(–1.06, –0.51)	(–1.39, –0.81)

Difference vs placebo, LS mean (SE)	–0.2 (0.2)	–0.1 (0.2)	–0.4 (0.2)
95% CI	(–0.58, 0.22)	(–0.45, 0.25)	(–0.78, –0.05)

Analyses are based on MMRM model with baseline randomization strata, baseline score, treatment, visit, and treatment-by-visit interaction.

CI, confidence interval; IV, intravenous; LBPI NRS, low back pain intensity numeric rating scale; LS, least squares; OA, osteoarthritis; PGA, patient global assessment; Q4W, every 4 weeks; Q8W, every 8 weeks; RMDQ, Roland-Morris Disability Questionnaire; SD, standard deviation; SE, standard error; SC, subcutaneous; TEAE, treatment-emergent adverse event.

Supplementary Table 3. Summary of TEAEs during the on-treatment period (safety analysis set)

		Fasinumab			
	Placebo (n=140)	**6 mg SC Q4W (n=139)**	**9 mg SC Q4W (n=139)**	**9 mg IV Q8W (n=140)**	**Combined (N=418)**
Patients with any TEAE, n (%)	94 (67.1%)	85 (61.2%)	95 (68.3%)	94 (67.1%)	274 (65.6%)
Patients with any serious TEAE, n (%)	4 (2.9%)	2 (1.4%)	3 (2.2%)	5 (3.6%)	10 (2.4%)
Patients with any severe TEAE, n (%)	5 (3.6%)	4 (2.9%)	2 (1.4%)	3 (2.1%)	9 (2.2%)
Patients with any TEAE leading to study drug discontinuation, n (%)	9 (6.4%)	5 (3.6%)	5 (3.6%)	5 (3.6%)	15 (3.6%)
Patients with any TEAE leading to study withdrawal, n (%)	10 (7.1%)	6 (4.3%)	2 (1.4%)	5 (3.6%)	13 (3.1%)
Patients with any TEAE leading to death, n (%)	0	0	0	0	0

IV, intravenous; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; TEAE, treatment-emergent adverse event.

Supplementary Table 4. Summary of AEs with >3% incidence during the post-treatment follow-up period by System Organ Class and Preferred Term (safety analysis set)

		Fasinumab			
Primary System Organ Class Preferred Term	**Placebo (n=140)**	**6 mg SC Q4W (n=139)**	**9 mg SC Q4W (n=139)**	**9 mg IV Q8W (n=140)**	**Combined (N=418)**
Number of post-treatment AEs	45	73	58	64	195
Patients with at least one post-treatment AE, n (%)	39 (27.9%)	42 (30.2%)	39 (28.1%)	44 (31.4%)	125 (29.9%)
Musculoskeletal and connective tissue disorders	20 (14.3%)	32 (23.0%)	28 (20.1%)	33 (23.6%)	93 (22.2%)
Arthralgia	13 (9.3%)	16 (11.5%)	9 (6.5%)	13 (9.3%)	38 (9.1%)
Back pain	4 (2.9%)	9 (6.5%)	12 (8.6%)	8 (5.7%)	29 (6.9%)
Pain in extremity	1 (0.7%)	7 (5.0%)	4 (2.9%)	10 (7.1%)	21 (5.0%)
Rapidly progressive osteoarthritis	1 (0.7%)	5 (3.6%)	4 (2.9%)	6 (4.3%)	15 (3.6%)
Musculoskeletal pain	2 (1.4%)	6 (4.3%)	3 (2.2%)	5 (3.6%)	14 (3.3%)
Infections and infestations	20 (14.3%)	17 (12.2%)	14 (10.1%)	14 (10.0%)	45 (10.8%)
Nasopharyngitis	7 (5.0%)	8 (5.8%)	7 (5.0%)	6 (4.3%)	21 (5.0%)
Upper respiratory tract infection	7 (5.0%)	5 (3.6%)	6 (4.3%)	2 (1.4%)	13 (3.1%)
Bronchitis	1 (0.7%)	3 (2.2%)	5 (3.6%)	4 (2.9%)	12 (2.9%)
Urinary tract infection	5 (3.6%)	1 (0.7%)	0	4 (2.9%)	5 (1.2%)

Post-treatment AEs included any AEs reported during the post-treatment follow-up period with an onset more than 4 weeks from the last dose of SC study drug or 8 weeks from the last dose of IV study drug.

MedDRA (Version 18.0) coding applied.

A patient who reported 2 or more AEs with the same preferred term is counted only once for that term.

A patient who reported 2 or more AEs with different preferred terms within the same system organ class is counted only once in that system organ class.

For system organ classes, the table is sorted by decreasing frequency in combined fasinumab group. Within each system organ class, preferred terms are sorted by decreasing frequency count in combined fasinumab group.

AE; adverse event; IV, intravenous; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous.

Dakin P, *et al*. *Ann Rheum Dis* 2020;0:1–9. doi: 10.1136/annrheumdis-2020-217259

Supplementary Table 5. Summary of SAEs during the on-treatment period by System Organ Class and Preferred Term (safety analysis set)

Primary System Organ Class Preferred Term	Placebo (n=140)	Fasinumab			
		6 mg SC Q4W (n=139)	9 mg SC Q4W (n=139)	9 mg IV Q8W (n=140)	Combined (N=418)
Number of serious TEAEs	4	4	3	5	12
Patients with at least one serious TEAE, n (%)	4 (2.9%)	2 (1.4%)	3 (2.2%)	5 (3.6%)	10 (2.4%)
Injury, poisoning and procedural complications	1 (0.7%)	1 (0.7%)	0	2 (1.4%)	3 (0.7%)
Concussion	0	1 (0.7%)	0	0	1 (0.2%)
Craniocerebral injury	0	1 (0.7%)	0	0	1 (0.2%)
Meniscus injury	0	0	0	1 (0.7%)	1 (0.2%)
Patella fracture	0	0	0	1 (0.7%)	1 (0.2%)
Skull fracture	0	1 (0.7%)	0	0	1 (0.2%)
Eye injury	1 (0.7%)	0	0	0	0
Cardiac disorders	0	1 (0.7%)	0	0	1 (0.2%)
Angina pectoris	0	1 (0.7%)	0	0	1 (0.2%)
General disorders and administration site conditions	0	0	0	1 (0.7%)	1 (0.2%)

Pyrexia	0	0	0	1 (0.7%)	1 (0.2%)
Infections and infestations	0	0	1 (0.7%)	0	1 (0.2%)
Diverticulitis	0	0	1 (0.7%)	0	1 (0.2%)
Musculoskeletal and connective tissue disorders	0	0	1 (0.7%)	0	1 (0.2%)
Osteoarthritis	0	0	1 (0.7%)	0	1 (0.2%)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 (0.7%)	0	0	1 (0.7%)	1 (0.2%)
Adenocarcinoma of colon	0	0	0	1 (0.7%)	1 (0.2%)
Tongue carcinoma stage IV	1 (0.7%)	0	0	0	0
Nervous system disorders	1 (0.7%)	0	1 (0.7%)	0	1 (0.2%)
Haemorrhagic stroke	0	0	1 (0.7%)	0	1 (0.2%)
Cerebrovascular accident	1 (0.7%)	0	0	0	0
Vascular disorders	0	0	0	1 (0.7%)	1 (0.2%)
Hypotension	0	0	0	1 (0.7%)	1 (0.2%)
Investigations	1 (0.7%)	0	0	0	0
Blood creatine phosphokinase increased	1 (0.7%)	0	0	0	0

MedDRA (Version 18.0) coding applied.

A patient who reported 2 or more TEAEs with the same preferred term is counted only once for that term.

A patient who reported 2 or more TEAEs with different preferred terms within the same system organ class is counted only once in that system organ class.

For SOCs, the table is sorted by decreasing frequency in combined fasinumab group. Within each SOC, PTs are sorted by decreasing frequency count in combined fasinumab group.

AE; adverse event; IV, intravenous; PT, preferred term; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; SOC, system organ class; TEAE, treatment-emergent adverse event.

Dakin P, *et al*. *Ann Rheum Dis* 2020;0:1–9. doi: 10.1136/annrheumdis-2020-217259

Supplementary Table 6. Summary of SAEs during the post-treatment follow-up period by System Organ Class and Preferred Term (safety analysis set)

Primary System Organ Class Preferred Term	Placebo (n=140)	Fasinumab			
		6 mg SC Q4W (n=139)	9 mg SC Q4W (n=139)	9 mg IV Q8W (n=140)	Combined (N=418)
Number of serious post-treatment AEs	7	9	7	12	28
Patients with at least one serious post-treatment AE, n (%)	6 (4.3%)	9 (6.5%)	6 (4.3%)	10 (7.1%)	25 (6.0%)
Musculoskeletal and connective tissue disorders	0	3 (2.2%)	3 (2.2%)	5 (3.6%)	11 (2.6%)
Rapidly progressive osteoarthritis	0	1 (0.7%)	1 (0.7%)	5 (3.6%)	7 (1.7%)
Back pain	0	2 (1.4%)	1 (0.7%)	0	3 (0.7%)
Synovial cyst	0	0	1 (0.7%)	0	1 (0.2%)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 (0.7%)	2 (1.4%)	0	2 (1.4%)	4 (1.0%)
Bladder cancer	0	0	0	1 (0.7%)	1 (0.2%)
Endometrial adenocarcinoma	0	0	0	1 (0.7%)	1 (0.2%)
Large intestine benign neoplasm	0	1 (0.7%)	0	0	1 (0.2%)
Mediastinum neoplasm	0	0	0	1 (0.7%)	1 (0.2%)
Small cell lung cancer metastatic	0	1 (0.7%)	0	0	1 (0.2%)

Lung neoplasm malignant	1 (0.7%)	0	0	0	0
Cardiac disorders	0	0	2 (1.4%)	0	2 (0.5%)
Atrial fibrillation	0	0	2 (1.4%)	0	2 (0.5%)
Infections and infestations	0	1 (0.7%)	0	1 (0.7%)	2 (0.5%)
Abscess limb	0	0	0	1 (0.7%)	1 (0.2%)
Septic shock	0	1 (0.7%)	0	0	1 (0.2%)
Injury, poisoning and procedural complications	1 (0.7%)	0	1 (0.7%)	1 (0.7%)	2 (0.5%)
Radius fracture	0	0	1 (0.7%)	0	1 (0.2%)
Stress fracture	0	0	0	1 (0.7%)	1 (0.2%)
Ulna fracture	0	0	1 (0.7%)	0	1 (0.2%)
Ankle fracture	1 (0.7%)	0	0	0	0
Nervous system disorders	0	2 (1.4%)	0	0	2 (0.5%)
Cervical radiculopathy	0	1 (0.7%)	0	0	1 (0.2%)
Multiple sclerosis	0	1 (0.7%)	0	0	1 (0.2%)
Psychiatric disorders	0	0	0	1 (0.7%)	1 (0.2%)
Personality disorder	0	0	0	1 (0.7%)	1 (0.2%)
Vascular disorders	0	1 (0.7%)	0	0	1 (0.2%)
Hypertension	0	1 (0.7%)	0	0	1 (0.2%)

Gastrointestinal disorders	2 (1.4%)	0	0	0	0
Intestinal obstruction	1 (0.7%)	0	0	0	0
Pancreatitis acute	1 (0.7%)	0	0	0	0
Hepatobiliary disorders	1 (0.7%)	0	0	0	0
Cholelithiasis	1 (0.7%)	0	0	0	0
Respiratory, thoracic and mediastinal disorders	1 (0.7%)	0	0	0	0
Haemoptysis	1 (0.7%)	0	0	0	0
Surgical and medical procedures	1 (0.7%)	0	0	0	0
Joint arthropathy	1 (0.7%)	0	0	0	0

MedDRA (Version 18.0) coding applied.

A patient who reported 2 or more AEs with the same preferred term is counted only once for that term.

A patient who reported 2 or more AEs with different preferred terms within the same system organ class is counted only once in that system organ class. For SOCs, the table is sorted by decreasing frequency in combined fasinumab group. Within each SOC, PTs are sorted by decreasing frequency count in combined fasinumab group.

AE; adverse event; IV, intravenous; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; SOC, system organ class.

Supplementary Table 7. Overview of AA events by treatment group, number of scheduled doses, screening K-L score and medical history (safety analysis set)

Treatment group	Number of scheduled doses received	Screening K-L score of affected joint(s)	Maximum K-L score of any joint	Medical history of OA	AA category	Days to first event
Placebo	2 (Day 1, Week 4)	3 (right hip)	4	Y	RPOA1 of the right hip	246
Fasinumab 6 mg SC Q4W	3 (Day 1, Week 4, Week 8)	2 (left knee)	3	Y	RPOA1 of the left knee	269
Fasinumab 6 mg SC Q4W	4 (Day 1, Week 4, Week 8, Week 12)	3 (left knee) 3 (right knee)	3	Y	RPOA1, RPOA2 of the left knee RPOA1, SIF of the right knee	250
Fasinumab 6 mg SC Q4W	3 (Day 1, Week 4, Week 8)	1 (right knee)	1	Y	RPOA1, SIF of right knee	324
Fasinumab 6 mg SC Q4W	4 (Day 1, Week 4, Week 8, Week 12)	2 (left knee) N/A (right shoulder)	3	Y	RPOA1 of the left knee RPOA1 of the right shoulder	251
Fasinumab 6 mg SC Q4W	1 (Day 1)	2 (left hip)	2	Y	RPOA1 of the left hip	259
Fasinumab 9 mg SC Q4W	3 (Day 1, Week 4, Week 8)	2 (right hip)	2	Y	RPOA1 of the right hip	253
Fasinumab 9 mg SC Q4W	4 (Day 1, Week 4, Week 8, Week 12)	2 (left hip)	3	N	RPOA1 of the left hip	379
Fasinumab 9 mg SC Q4W	2 (Day 1, Week 4)	2 (left knee)	2	N	RPOA1 of the left knee	132
Fasinumab 9 mg SC Q4W	2 (Day 1, Week 4)	1 (left knee)	1	Y	RPOA1, SIF of the left knee	254

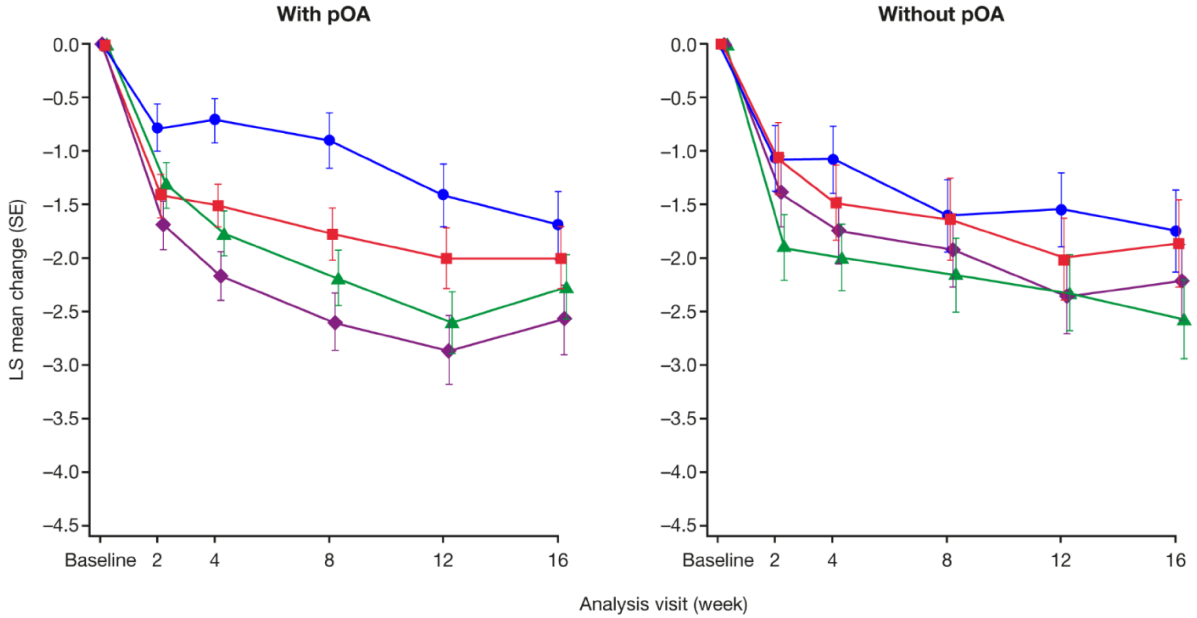
Fasinumab 9 mg IV Q8W	2 (Day 1, Week 8)	2 (right knee)	2	Y	RPOA1 of the right knee	254
Fasinumab 9 mg IV Q8W	2 (Day 1, Week 8)	2 (right knee)	2	Y	RPOA1 of the right knee	280
Fasinumab 9 mg IV Q8W	1 (Day 1)	3 (right hip) N/A (right shoulder)	3	Y	RPOA1 of the right hip RPOA1 of the right shoulder	106
Fasinumab 9 mg IV Q8W	2 (Day 1, Week 8)	3 (right knee)	3	Y	RPOA1 of the right knee	448
Fasinumab 9 mg IV Q8W	2 (Day 1, Week 8)	0 (right knee)	2*	N	RPOA1 of the right knee	398
Fasinumab 9 mg IV Q8W	2 (Day 1, Week 8)	3 (left knee)	3	Y	RPOA2 of the left knee	93
Fasinumab 9 mg IV Q8W	2 (Day 1, Week 8)	3 (left knee)	3	Y	SIF of the left knee	134

*Patient included in non-pOA subgroup; all other patients with AA events were included in the pOA subgroup based on medical history of OA and/or K-L score ≥2 in hip or ≥3 in knee.

K-L scores at screening were only assessed for hip and knee joints; in two shoulder joints, screening radiographs documented one with moderate OA and one with severe OA.

AA, adjudicated arthropathy; IV, intravenous; K-L, Kellgren-Lawrence; OA, osteoarthritis; Q4W, every 4 weeks; Q8W, every 8 weeks; RPOA1, rapid progressive OA type 1; RPOA2, rapid progressive OA type 2; SC, subcutaneous; SIF, subchondral insufficiency fracture.

Supplementary Figure 1. Least squares mean change from baseline in average daily LBPI NRS score by pOA subgroup (mITT analysis set)

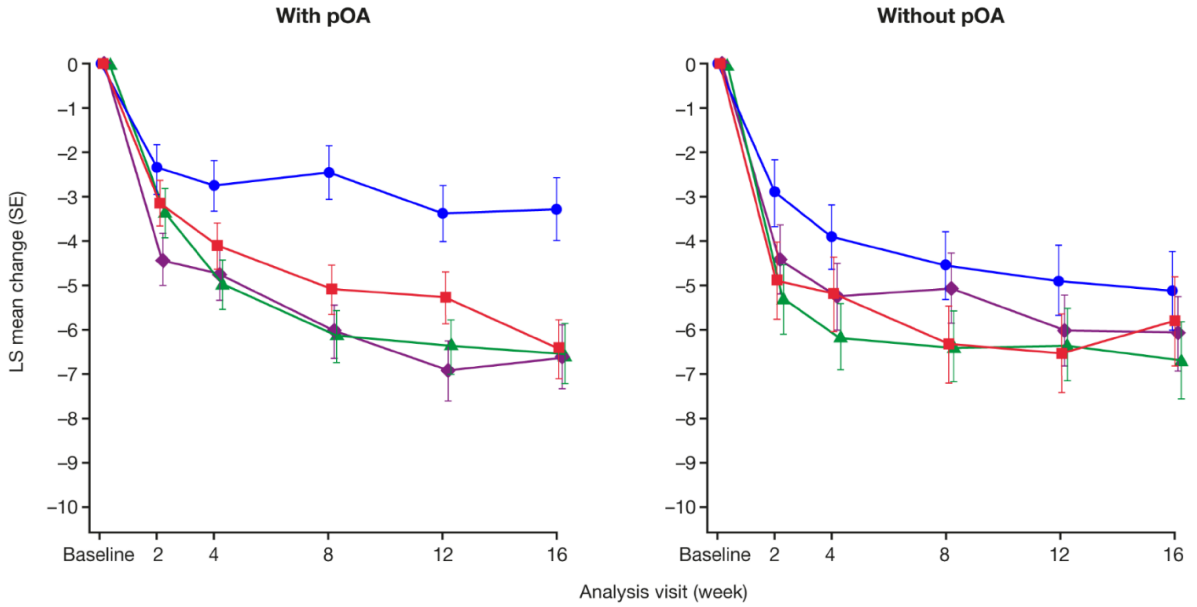


	Baseline	Week 2		Week 4		Week 8		Week 12		Week 16		Baseline	Week 2		Week 4		Week 8		Week 12		Week 16	
	N	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	N	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)
Placebo	81	78	−0.8 (0.21)	77	−0.7 (0.21)	54	−0.9 (0.25)	40	−1.4 (0.29)	31	−1.7 (0.30)	58	58	−1.1 (0.30)	56	−1.1 (0.30)	41	−1.6 (0.33)	29	−1.5 (0.34)	18	−1.7 (0.37)
Fasinumab 6 mg SC Q4W	90	87	−1.4 (0.20)	87	−1.5 (0.19)	61	−1.8 (0.24)	42	−2.0 (0.27)	32	−2.0 (0.29)	47	46	−1.1 (0.34)	45	−1.5 (0.34)	37	−1.6 (0.37)	27	−2.0 (0.37)	16	−1.9 (0.40)
Fasinumab 9 mg SC Q4Wa	68	67	−1.7 (0.22)	61	−2.2 (0.22)	51	−2.6 (0.26)	32	−2.9 (0.31)	26	−2.6 (0.32)	71	68	−1.4 (0.31)	67	−1.7 (0.31)	54	−1.9 (0.34)	42	−2.4 (0.34)	29	−2.2 (0.35)
Fasinumab 9 mg IV Q8W	78	76	−1.3 (0.21)	74	−1.8 (0.21)	59	−2.2 (0.25)	43	−2.6 (0.28)	34	−2.3 (0.29)	62	62	−1.9 (0.30)	58	−2.0 (0.31)	44	−2.2 (0.34)	33	−2.3 (0.34)	22	−2.6 (0.37)

pOA defined by medical history and/or K-L score ≥2 in hip or ≥3 in knee.

IV, intravenous; K-L, Kellgren-Lawrence; LBPI NRS, low back pain intensity numeric rating scale; LSM, least squares mean; mITT, modified intent-to-treat; pOA, peripheral osteoarthritis; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; SE, standard error.

Supplementary Figure 2. Least squares mean change from baseline in RMDQ total score by pOA subgroup (mITT analysis set)

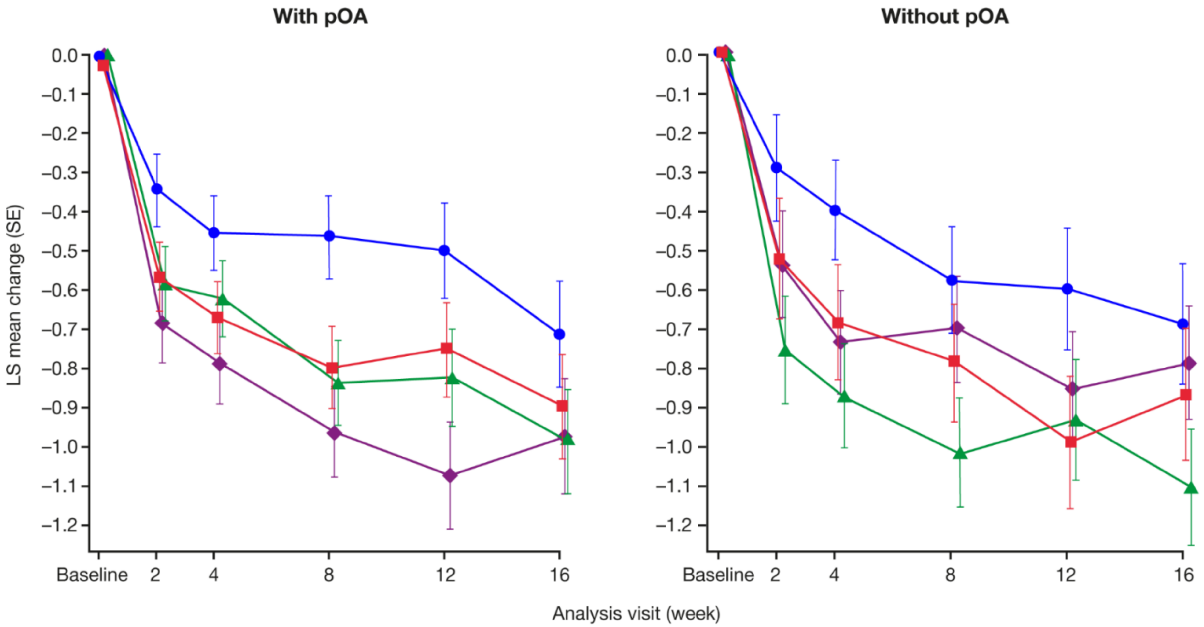


	With pOA										Without pOA									
	Baseline	Week 2		Week 4		Week 8		Week 12		Week 16	Baseline	Week 2		Week 4		Week 8		Week 12		Week 16	
	N	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	N	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)
Placebo	74	70	−2.4 (0.55)	70	−2.7 (0.55)	50	−2.4 (0.59)	37	−3.4 (0.63)	28	−3.3 (0.69)	58	58	−2.9 (0.73)	57	−3.9 (0.72)	42	−4.5 (0.76)	30	−4.9 (0.78)	18	−5.1 (0.87)
Fasinumab 6 mg SC Q4W	90	87	−3.1 (0.50)	85	−4.1 (0.50)	61	−5.1 (0.54)	40	−5.3 (0.59)	31	−6.4 (0.64)	45	45	−4.9 (0.86)	42	−5.2 (0.84)	36	−6.3 (0.86)	26	−6.5 (0.89)	15	−5.8 (0.98)
Fasinumab 9 mg SC Q4W	67	65	−4.4 (0.57)	61	−4.7 (0.58)	50	−6.0 (0.60)	32	−6.9 (0.66)	26	−6.6 (0.71)	69	69	−4.4 (0.76)	65	−5.2 (0.75)	52	−5.0 (0.77)	41	−6.0 (0.79)	29	−6.1 (0.83)
Fasinumab 9 mg IV Q8W	75	72	−3.4 (0.54)	71	−5.0 (0.55)	57	−6.1 (0.57)	41	−6.4 (0.61)	32	−6.5 (0.66)	61	61	−5.3 (0.76)	57	−6.2 (0.75)	44	−6.4 (0.78)	33	−6.3 (0.80)	23	−6.7 (0.86)

pOA defined by medical history and/or K-L score ≥2 in hip or ≥3 in knee.

IV, intravenous; K-L, Kellgren-Lawrence; LSM, least squares mean; mITT, modified intent-to-treat; pOA, peripheral osteoarthritis; Q4W, every 4 weeks; Q8W, every 8 weeks; RMDQ, Roland-Morris Disability Questionnaire; SC, subcutaneous; SE, standard error.

Supplementary Figure 3. Least squares mean change from baseline in PGA of LBP score by pOA subgroup (mITT analysis set)



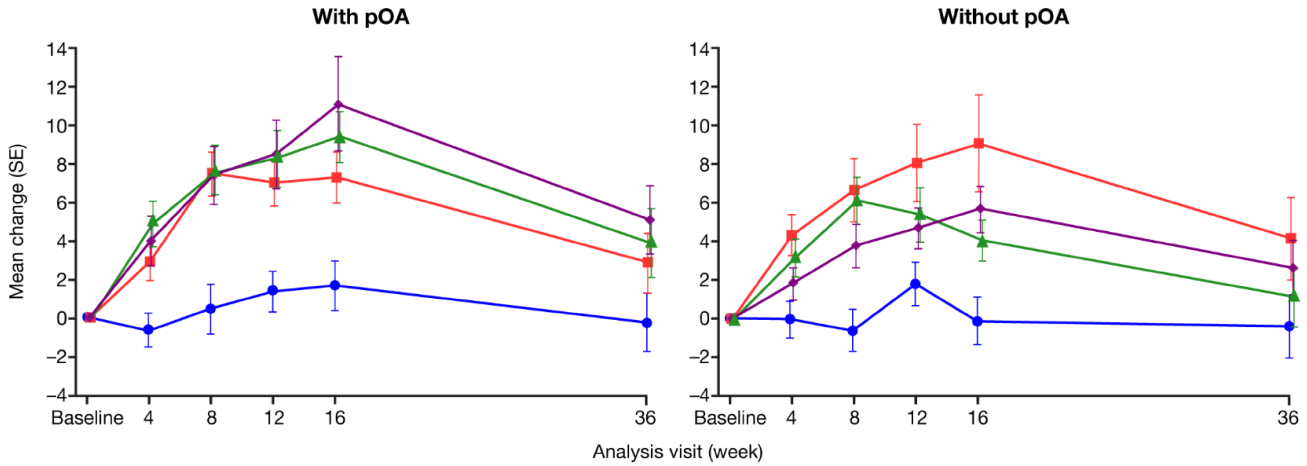
	Baseline	Week 2		Week 4		Week 8		Week 12		Week 16	
	N	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)
Placebo	82	78	−0.3 (0.09)	78	−0.5 (0.10)	58	−0.5 (0.11)	42	−0.5 (0.12)	32	−0.7 (0.13)
Fasinumab 6 mg SC Q4W	92	89	−0.6 (0.09)	87	−0.7 (0.09)	63	−0.8 (0.10)	42	−0.8 (0.12)	33	−0.9 (0.13)
Fasinumab 9 mg SC Q4W	68	66	−0.7 (0.10)	62	−0.8 (0.10)	51	−1.0 (0.11)	32	−1.1 (0.14)	26	−1.0 (0.15)
Fasinumab 9 mg IV Q8W	78	75	−0.6 (0.09)	74	−0.6 (0.10)	60	−0.8 (0.11)	43	−0.8 (0.12)	34	−1.0 (0.13)

	Baseline	Week 2		Week 4		Week 8		Week 12		Week 16	
	N	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)	n	LSM (SE)
Placebo	58	58	−0.3 (0.13)	57	−0.4 (0.13)	42	−0.6 (0.14)	30	−0.6 (0.15)	18	−0.7 (0.15)
Fasinumab 6 mg SC Q4W	47	46	−0.5 (0.15)	44	−0.7 (0.14)	38	−0.8 (0.15)	27	−1.0 (0.17)	15	−0.9 (0.17)
Fasinumab 9 mg SC Q4W	71	69	−0.5 (0.13)	67	−0.7 (0.13)	54	−0.7 (0.13)	43	−0.9 (0.15)	29	−0.8 (0.14)
Fasinumab 9 mg IV Q8W	62	61	−0.8 (0.14)	58	−0.9 (0.13)	44	−1.0 (0.14)	33	−0.9 (0.15)	23	−1.1 (0.15)

pOA defined by medical history and/or K-L score ≥2 in hip or ≥3 in knee.

IV, intravenous; K-L, Kellgren-Lawrence; LSM, least squares mean; mITT, modified intent-to-treat; PGA of LBP, Patient Global Assessment of Lower Back Pain; pOA, peripheral osteoarthritis; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; SE, standard error.

Supplementary Figure 4. Mean change from baseline in alkaline phosphatase (U/L) by pOA subgroup (safety analysis set)



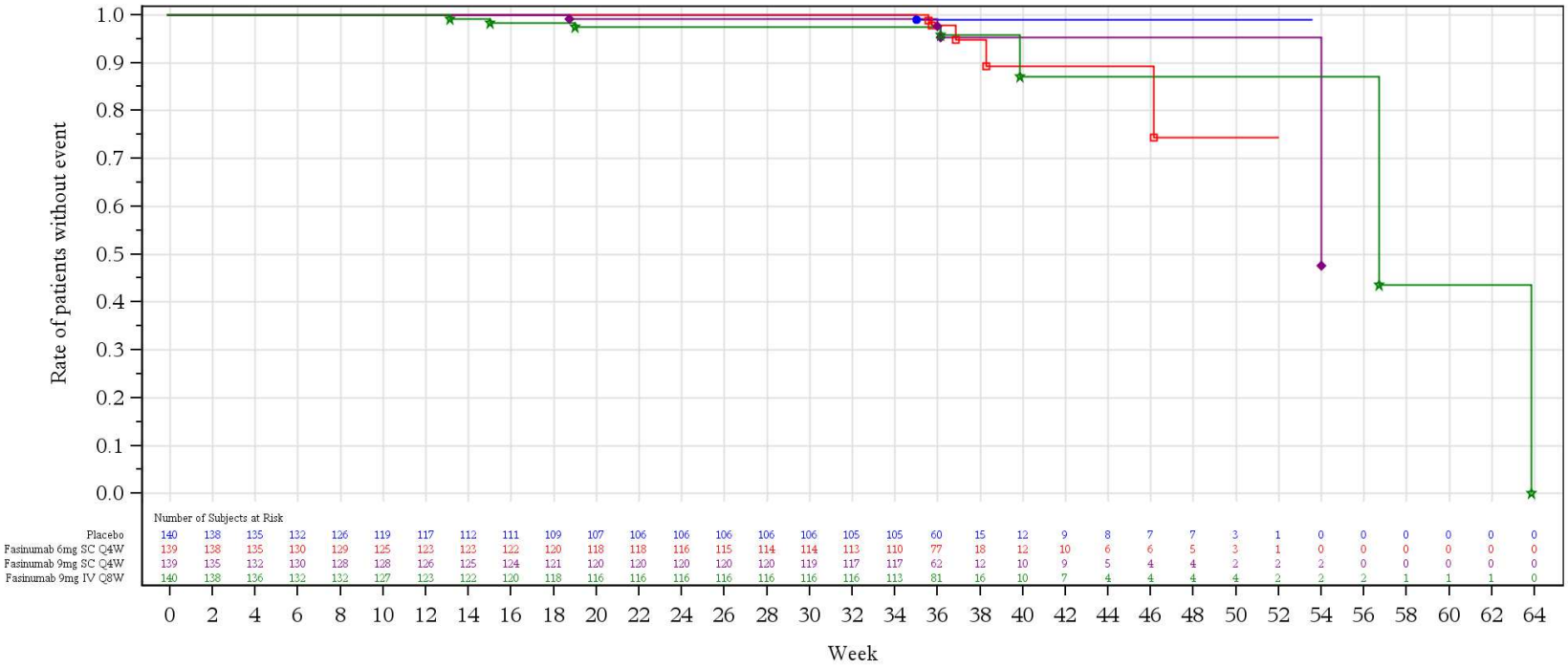
	Baseline	Week 4		Week 8		Week 12		Week 16		Week 36	
	N	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)
Placebo	82	77	−0.6 (0.83)	71	0.5 (1.28)	67	1.4 (1.06)	64	1.7 (1.28)	59	−0.2 (1.48)
Fasinumab 6 mg SC Q4W	92	87	2.9 (0.90)	83	2.0 (1.13)	78	7.0 (1.15)	75	7.3 (1.43)	72	2.9 (1.45)
Fasinumab 9 mg SC Q4W	68	63	4.0 (1.26)	62	7.4 (1.46)	59	8.5 (1.73)	60	11.1 (2.41)	54	5.1 (1.78)
Fasinumab 9 mg IV Q8W	78	72	4.9 (1.17)	69	7.7 (1.29)	70	8.3 (1.45)	67	9.4 (1.27)	69	3.9 (1.73)

	Baseline	Week 4		Week 8		Week 12		Week 16		Week 36	
	N	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)
Placebo	58	55	0.0 (0.98)	53	−0.6 (1.13)	47	2.0 (1.17)	44	−0.1 (1.30)	41	−0.4 (1.75)
Fasinumab 6 mg SC Q4W	47	45	4.7 (1.13)	42	7.2 (1.76)	39	8.7 (2.11)	38	9.8 (2.68)	36	4.5 (2.27)
Fasinumab 9 mg SC Q4W	71	67	2.0 (0.86)	66	4.1 (1.22)	64	5.1 (1.11)	61	6.1 (1.27)	62	2.9 (1.47)
Fasinumab 9 mg IV Q8W	62	58	3.4 (1.04)	57	6.6 (1.30)	54	5.8 (1.48)	51	4.4 (1.12)	48	1.2 (1.57)

pOA defined by medical history and/or K-L score ≥2 in hip or ≥3 in knee.

IV, intravenous; K-L, Kellgren-Lawrence; mITT, modified intent-to-treat; pOA, peripheral osteoarthritis; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous; SE, standard error; U/L, units per litre.

Supplementary Figure 5. Kaplan-Meier curve of time to event for patients with AA events (safety analysis set)



AA, adjudicated arthropathy; IV, intravenous; Q4W, every 4 weeks; Q8W, every 8 weeks; SC, subcutaneous.