

Intradiscal Glucocorticoid Injection for Patients With Chronic Low Back Pain Associated With Active Discopathy

A Randomized Trial

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Background: Active discopathy is associated with a specific phenotype of chronic low back pain (LBP). Local inflammation has a role in active discopathy-associated symptoms.

Objective: To assess the efficacy of a single glucocorticoid intradiscal injection (GC IDI) in patients with chronic LBP with active discopathy.

Design: Prospective, parallel-group, double-blind, randomized, controlled study. (ClinicalTrials.gov: NCT00804531)

Setting: 3 tertiary care centers in France.

Patients: 135 patients with chronic LBP with active discopathy on magnetic resonance imaging (MRI).

Intervention: A single GC IDI (25 mg prednisolone acetate) during discography ($n = 67$) or discography alone ($n = 68$).

Measurements: The primary outcome was the percentage of patients with LBP intensity less than 40 on an 11-point numerical rating scale (0 [no pain] to 100 [maximum pain] in 10-point increments) in the previous 48 hours at 1 month after the intervention. The main secondary outcomes were LBP intensity and persistent active discopathy on MRI at 12 months and spine-specific

limitations in activities, health-related quality of life, anxiety and depression, employment status, and use of analgesics and non-steroidal anti-inflammatory drugs at 1 and 12 months.

Results: All randomly assigned patients were included in the primary efficacy analysis. At 1 month after the intervention, the percentage of responders (LBP intensity <40) was higher in the GC IDI group (36 of 65 [55.4%]) than the control group (21 of 63 [33.3%]) (absolute risk difference, 22.1 percentage points [95% CI, 5.5 to 38.7 percentage points]; $P = 0.009$). The groups did not differ in LBP intensity at 12 months and in most secondary outcomes at 1 and 12 months.

Limitation: Tertiary care setting.

Conclusion: In chronic LBP associated with active discopathy, a single GC IDI reduces LBP at 1 month but not at 12 months.

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Chronic low back pain (LBP) is a common cause of long-term disability (1). Identifying subgroups of patients with specific causative lesions who could benefit from targeted therapies is challenging (2). In the late 1980s, Modic and colleagues used magnetic resonance imaging (MRI) to classify vertebral endplate subchondral bone changes adjacent to degenerative disc disease into 3 groups: Modic 1 (characterized by vertebral endplate subchondral bone edema), Modic 2 (characterized by fatty degeneration), and Modic 3 (characterized by fibrotic changes) (3). Modic 1 changes are rarely observed in asymptomatic patients without degenerative disc disease but are detected in up to 46% of patients with chronic LBP (4–6). Modic 1 lesions are associated with poor chronic LBP outcomes (7), but Modic 2 and 3 are considered more quiescent stages of the same dynamic process (2). Further phenotyping of patients with Modic 1-associated chronic LBP has revealed specific clinical and biological features, including inflammatory-like chronic LBP (8–10) and low-grade systemic (10) and local inflammation (11), which supports a concept of “active discopathy” (2, 12). These findings provide a sound rationale for the evaluation of treatments targeting local inflammation, such as glucocorticoid intradiscal injection (GC IDI).

In 2 prospective, double-blind, randomized, controlled studies, GC IDI did not reduce discogenic LBP at 2 weeks (13) or 1 year (14), but patients were included regardless of Modic changes (13, 14). Open-label studies have suggested that GC IDI could provide short-term relief in patients with Modic-associated chronic LBP and that Modic 1 changes could be predictive of a better response to GC IDI than other Modic types (15–18). Accelerated switching from Modic 1 to a normal vertebral endplate subchondral bone MRI signal after GC IDI has also been reported (19). A double-blind, randomized, controlled study of 120 patients with Modic-associated chronic LBP receiving GC IDI showed reduced LBP intensity at 3 and 6 months. Patients with Modic 1 or 2 changes were included in the study, but the Modic 1 sample was small ($n = 60$) (20).

See also:

Editorial comment	1
Summary for Patients	2
Web-Only	
Supplement	

Despite consistent evidence supporting the role of local inflammation in the pathogenesis of active discopathy-related symptoms, large high-quality clinical trials assessing the short-term efficacy of GC IDI in patients with chronic LBP with active discopathy are lacking. We hypothesized that Modic 1 changes could reflect an “inflammatory flare” of degenerative disc disease. To that end, we compared the efficacy of a single GC IDI during discography versus discography alone for pain intensity at 1 month in patients with chronic LBP associated with active discopathy, for whom first-line conservative treatments had failed.

METHODS

Design Overview

We conducted a prospective, parallel-group, double-blind, randomized, controlled, multicenter study. Recruitment started on 4 April 2009, and follow-up was completed on 17 June 2014. Patients were allocated in a 1:1 ratio. Patients, treating physicians, data collectors, and statisticians were blinded to allocation, but radiologists were not. The study was approved by our institutional review board (Comité Consultatif de Protection des Personnes en Recherche Biomédicale d’Île-de-France, CPP2233), and all participants gave written consent. An English translation of the Methods section of the original protocol, including the original statistical analysis plan and a summary of changes and the reasons for them, is provided in the **Supplement** (available at Annals.org); changes made to the methods after the trial began are summarized in **Appendix Table 1** (available at Annals.org). Several errors occurred during trial registration: “Fears-avoidance belief” and “coping strategies” were first registered as secondary efficacy outcomes but were collected at baseline only (corrected on 6 May 2015), and safety outcomes have not been registered but are reported in the current article. These errors did not affect patients, and no interim analyses were performed (**Appendix Table 1**).

Setting and Participants

The study was conducted in the Physical Medicine and Rehabilitation and Rheumatology departments of 3 tertiary care centers in France with expertise in the management of spinal disorders (Cochin and Lariboisière Hospitals in Paris and Lille Hospital). Patients who were referred to the investigating centers for management of their chronic LBP were identified and screened for eligibility. Eligibility criteria were daily LBP for at least 3 months, with mean intensity greater than 40 on an 11-point numerical rating scale (NRS) (0 [no pain] to 100 [maximum pain] in 10-point increments) in the previous 48 hours and lumbar Modic 1 changes on MRI for less than 6 months (defined as vertebral endplate subchondral bone hypointense signal in T1-weighted sequence and hyperintense signal in T2-weighted sequence, adjacent to degenerative disc disease). A complete description of the inclusion and

exclusion criteria is presented in **Appendix Table 2** (available at Annals.org).

Randomization and Interventions

An independent statistician provided a computer-generated randomization list, with permuted blocks of fixed size 4 stratified by center. Numbered treatment boxes were sent to the pharmacies of the 3 investigating centers according to the randomization list and the size of the blocks. At enrollment, patients were randomly assigned and were given a treatment number by staff at the Clinical Research Unit (Unité de Recherche Clinique Paris Centre). On the day of the intervention, the pharmacy prefilled a syringe with the appropriate product according to the randomization assignment and hand-delivered the numbered treatment box containing the prefilled syringe to the radiology department.

Eight board-certified radiologists (5 at Cochin Hospital, 2 at Lariboisière Hospital, and 1 at Lille Hospital) with expertise in administering IDIs performed the interventions. Radiologists were trained by the study investigators to administer the IDI in a standardized manner under fluoroscopic control and strict aseptic conditions, as previously described (16). Briefly, patients were placed in a lateral decubitus position, and the IDI involved a posterolateral approach with use of a coaxial device (88.9-mm 18G spinal needle and 198-mm 22G disc needle). During incremental progression of the needle, needle-tip positioning and orientation in lateral and frontal plans were assessed by sequential fluoroscopic imaging. The GC IDI group received a single injection of 1 mL of iodixanol contrast (Visipaque 320 [GE Healthcare]) and 1 mL (25 mg) of prednisolone acetate (Hydrocortancyl 2.5% [Aventis]), and the control group received a single IDI of 1 mL of iodixanol contrast, both at the lumbar level of Modic 1 changes. No anesthetic was injected in the intervertebral disc, and antibiotic prophylaxis was not used.

Because the volume and color of the product differed between groups (2 mL of white fluid in the GC IDI group and 1 mL of transparent fluid in the control group), the radiologists were not blinded. They were told not to communicate with patients, treating physicians, or other study personnel about the treatment.

Outcomes and Follow-up

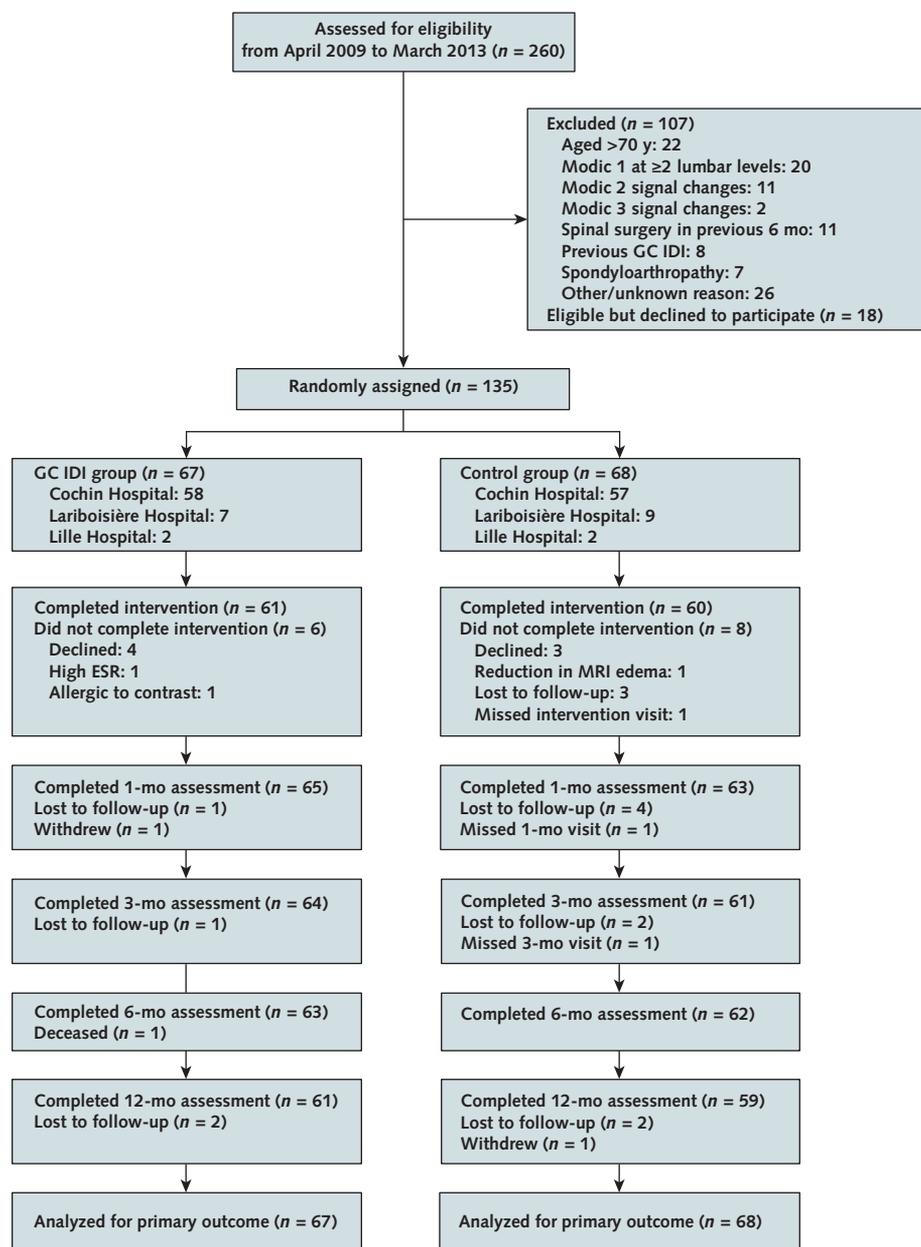
The primary efficacy outcome was the percentage of patients with LBP intensity less than 40 on an 11-point NRS in the previous 48 hours at 1 month after the intervention. This cutoff corresponds to the patient acceptable symptom state in chronic LBP (21). Secondary efficacy outcomes were LBP intensity on an NRS and persistent active discopathy on MRI at 12 months, as well as spine-specific limitations in activities (assessed with the Quebec Back Pain Disability Scale, with scores ranging from 0 [no limitations] to 100 [maximum limitations]), health-related quality of life (assessed with the Physical Component Summary and Mental Component Summary of the Medical Outcomes Study Short Form-12, with scores ranging from 0 [worst] to 100 [best]), anxiety and depression symptoms (assessed with the

Hospital Anxiety and Depression Scale [HADS], with scores ranging from 0 [no clinically significant symptoms] to 21 [maximum clinically significant symptoms]), self-reported use of analgesics and nonsteroidal anti-inflammatory drugs in the previous week, employment status (inactive, sick leave, invalidism, retired, or unemployed), and changes in LBP-related limitations in activities (worse, identical, slightly improved, improved, highly improved, or resolved), all at 1 and 12 months. All of the primary and secondary efficacy outcomes that we assessed are reported in this article.

Baseline data were collected at randomization, and other assessments were done before the intervention was administered and at 1, 3, 6, and 12 months. All primary and secondary outcomes were assessed during face-to-face visits.

Safety outcomes were collected during the intervention and at 48 hours and 12 months. During the IDI, the radiologist recorded the following symptoms: LBP provocation, mean intensity, localized bleeding, postintervention increase in intensity, and adverse events. Patients also were asked whether they would agree to a

Figure 1. Enrollment, randomization, and follow-up.



ESR = erythrocyte sedimentation rate; GC IDI = glucocorticoid intradiscal injection; MRI = magnetic resonance imaging.

second IDI, and the acceptability of the intervention was assessed on an 11-point NRS (0 [not acceptable] to 10 [totally acceptable]). Unspecified technical difficulties and proper needle positioning were recorded (Appendix Table 3, available at [Annals.org](#)). The success of blinding was assessed using the Credibility/Expectancy Questionnaire immediately after the intervention (Appendix Table 4, available at [Annals.org](#)).

At 48 hours and 12 months after the intervention, an investigator blinded to group allocation recorded symptoms and adverse effects by using open-ended questions (Appendix Table 5, available at [Annals.org](#)). Serious adverse events were reviewed by 2 independent blinded investigators. Events were classified into 4 categories: 1) hospitalizations for usual care of chronic LBP, defined as hospitalizations for multidisciplinary rehabilitation programs that could include spinal injections other than GC IDI, physiotherapy, occupational therapy, lumbar bracing, or psychological factors management, without evidence of events possibly related to the GC IDI, such as disc calcification or spondylodiscitis; 2) hospitalizations for events unrelated to chronic LBP; 3) events unrelated to chronic LBP without hospitalization; and 4) events possibly related to the IDI.

Imaging safety outcomes were also recorded, specifically intervertebral disc calcifications and loss of disc height (millimeters and percentage) on at least 1 radiograph at 12 months. An independent radiologist compared baseline and 12-month lumbar radiographs (lateral views) and MRI scans (T1-weighted and short tau inversion recovery-weighted sequences) at the level of the active discopathy in a standardized and blinded manner. For loss of disc height, the intraobserver intraclass correlation coefficient was 0.86 (95% CI, 0.76 to 0.92).

Statistical Analysis

With an α risk of 0.05, a power ($1 - \beta$) of 0.80, and a predicted difference of 20 percentage points (30% in the GC IDI group vs. 10% in the control group) in the proportion of patients with LBP intensity less than 40 on an NRS at 1 month after the intervention, we calculated that 62 participants were needed in each group. Estimating that 10% of patients would be lost to follow-up or would not receive the allocated intervention, we sought to include 67 patients in each group. Categorical variables are presented as frequencies and percentages, and quantitative variables are presented as means and SDs, means and 95% CIs, or medians and interquartile ranges.

The primary efficacy analysis was conducted as an intention-to-treat analysis: All randomly assigned patients were analyzed for the primary outcome in their randomization group. Missing data for the primary binary outcome were imputed by multiple imputation using chained equations and a missing-at-random assumption, which allowed for separation of conditional distributions for each imputed variable. Missing data for any of the covariates used in the multiple imputation model also were imputed. Predictive mean matching

was used for quantitative variables and logistic regression was used for binary variables, with a mean of 20 imputations. The covariates used to generate the multiple imputed data sets were age, sex, educational level, employment status, LBP and radicular pain intensity, Quebec score, and HADS anxiety and depression scores at enrollment. Imputed values for the primary outcome were binary (LBP intensity <40 or ≥ 40).

Logistic regression models with fixed center and treatment effects were used to assess between-group differences for binary efficacy outcomes at 1 and 12 months. The marginal standardization approach was used to obtain estimates of response, absolute risk differences, and relative risks and corresponding 95% CIs.

To compare between-group differences in mean change from baseline for quantitative repeated efficacy outcomes, a constrained longitudinal data analysis was used (22–24). This mixed model uses a constrained full-likelihood approach, whereby both the baseline and postbaseline values are modeled as dependent variables. The model assumes that both the baseline and postbaseline measurements are jointly multivariate and normally distributed because the baseline value is treated as part of the response vector. The true baseline means are constrained to be the same for both treatment groups. The constrained longitudinal data analysis model can include all randomly assigned participants with a baseline or postbaseline value. Such methods that are based on maximum likelihood are consistent under the missing-at-random assumption; hence, this analysis provides an adjustment for the observed baseline difference in estimating treatment efficacy. Random effects at the patient level and fixed effects at the center level were added to these models. Results are expressed as differences in mean change from baseline with 95% CIs at 1 and 12 months. In a sensitivity analysis to support the primary binary end point, the NRS pain score at 1 month was also analyzed using the constrained longitudinal data analysis model.

All statistical tests were 2-sided, and a P value less than 0.05 was considered statistically significant. Data were analyzed using the MI (multiple imputation) and MIXED (constrained longitudinal data analysis model) procedures in SAS, versions 9.3 and 9.4 (SAS Institute). Other analyses were performed using R, version 3.2.2 (R Foundation for Statistical Computing); logistic regressions using marginal standardization were performed with the `glm` function and the `stdReg` package, and multiple imputations for the primary outcome analysis were combined with the `mice` package.

Role of the Funding Source

The study was funded by a research grant from the French Ministry of Health (Programme Hospitalier de Recherche Clinique, project no. P070157) and sponsored by the Département de la Recherche Clinique et du Développement de l'Assistance Publique-Hôpitaux de Paris. The funding source was not involved in the study design, data collection or interpretation, statistical analysis, manuscript preparation, or the decision to submit the manuscript for publication.

Table 1. Baseline Characteristics of Patients With Chronic LBP Associated With Active Discopathy*

Characteristic	GC IDI Group (n = 67)	Control Group (n = 68)	All Patients (n = 135)
Median age (IQR), y	46.0 (42.0-54.0)	47.0 (41.0-53.5)	46.0 (42.0-54.0)
Female, n/N (%)	38/67 (56.7)	44/68 (64.7)	82/135 (60.7)
Median body mass index (IQR), kg/m ²	24.4 (22.3-27.8)	24.6 (22.4-27.4)	24.5 (22.4-27.7)
History of lumbar surgery, n/N (%)	10/67 (14.9)	9/68 (13.2)	19/135 (14.1)
History of nucleolysis at the level of active discopathy, n/N (%)	2/67 (3.0)	0/68 (0)	2/135 (1.5)
Educational level, n/N (%)			
High school or less	38/66 (57.6)	33/68 (48.5)	71/135 (53.0)
Higher education	28/66 (42.4)	35/68 (51.5)	63/135 (47.0)
Employment status, n/N (%)			
Full- or part-time employment	39/67 (58.2)	36/68 (52.9)	75/135 (55.6)
Unemployed	0/67 (0)	3/68 (4.4)	3/135 (2.2)
Sick leave	19/67 (28.4)	25/68 (36.8)	44/135 (32.6)
Invalidism	5/67 (7.5)	1/68 (1.5)	6/135 (4.4)
Retired	4/67 (6.0)	3/68 (4.4)	7/135 (5.2)
Mean LBP intensity on NRS (SD) (range, 0-100)†	69.6 (13.5)	67.6 (14.4)	68.6 (13.9)
Mean radicular pain intensity on NRS (SD) (range, 0-100)†	37.5 (26.5)	30.9 (26.0)	34.1 (26.4)
Mean chronic LBP duration (SD), y	6.6 (6.0)	6.1 (5.2)‡	6.3 (5.6)
Mean current LBP episode duration (SD), y	1.4 (1.4)	1.3 (1.0)	1.3 (1.2)
Median morning stiffness duration (IQR), min	30.0 (10.0-60.0)	30.0 (5.0-45.0)‡	30.0 (10.0-60.0)
Morning stiffness >20 min, n/N (%)	34/67 (50.7)	34/67 (50.7)	68/134 (50.7)
Nighttime awakenings, n/N (%)	47/67 (70.1)	51/68 (75.0)	98/135 (72.6)
Morning stiffness and/or nighttime awakenings, n/N (%)	53/67 (79.1)	61/68 (89.7)	114/135 (84.4)
Median modified Schober test score (IQR), cm	20.0 (19.0-21.0)	20.0 (19.0-21.0)	20.0 (19.0-21.0)
Median finger-to-floor test score (IQR), cm	24.0 (8.0-35.0)	17.0 (3.0-30.0)	19.0 (5.0-33.0)
Previous treatments, n/N (%)			
Analgesics	66/67 (98.5)	67/67 (100.0)	133/134 (99.3)
Nonopioids	52/65 (80.0)	57/64 (89.1)	109/129 (84.5)
Weak opioids§	59/65 (90.8)	55/64 (85.9)	114/129 (88.4)
Strong opioids§	19/65 (29.2)	11/64 (17.2)	30/129 (23.3)
Nonsteroidal anti-inflammatory drugs	66/67 (98.5)	67/67 (100.0)	133/134 (99.3)
Muscle relaxants	45/66 (68.2)	41/67 (61.2)	86/133 (64.7)
≥1 epidural injection	48/67 (71.6)	49/66 (74.2)	97/133 (72.9)
≥1 facet joint injection	33/66 (50.0)	32/66 (48.5)	65/132 (49.2)
Lumbar brace	62/67 (92.5)	56/67 (83.6)	118/134 (88.1)
Physiotherapy	58/67 (86.6)	60/67 (89.6)	118/134 (88.1)
Rehabilitation program	24/67 (35.8)	27/66 (40.9)	51/133 (38.3)
Mean QBPDS score (SD) (range, 0-100)	50.3 (15.4)¶	48.1 (14.5)**	49.2 (14.9)
Mean SF-12 score (SD) (range, 0-100)††			
Physical component	31.6 (6.9)¶	32.4 (7.3)**	32.0 (7.1)
Mental component	36.6 (10.5)¶	38.1 (10.1)**	37.4 (10.3)
Mean HADS score (SD) (range, 0-21)‡‡			
Anxiety	10.9 (4.3)**	10.4 (3.5)**	10.6 (3.9)
Depression	7.4 (3.6)**	7.1 (3.9)**	7.3 (3.8)
Median FABQ score (IQR)§§			
Physical activity (range, 0-24)	17.0 (12.0-21.0)¶	16.0 (12.0-20.0)¶	16.0 (12.0-20.0)
Work (range, 0-42)	24.0 (11.0-35.0)	21.0 (10.0-30.0)¶¶	22.0 (11.0-33.0)
Median CSQ score (IQR)***			
Distraction (range, 5-20)	13.0 (8.0-17.0)¶¶¶	13.0 (11.0-16.0)¶¶	13.0 (10.0-16.0)
Catastrophizing (range, 5-20)	14.0 (12.0-17.0)	14.0 (10.0-17.0)	14.0 (11.0-17.0)
Ignoring pain sensations (range, 4-16)	10.0 (7.0-12.0)	9.0 (8.0-12.0)**	9.0 (8.0-12.0)
Distancing from pain (range, 4-16)	7.0 (5.0-10.0)¶¶¶	7.0 (4.0-11.0)†††	7.0 (4.0-11.0)
Coping self-statements (range, 8-32)	24.0 (21.0-28.0)¶¶¶	26.0 (23.0-28.0)**	25.0 (22.0-28.0)
Praying (range, 3-12)	5.0 (3.0-9.0)¶¶	4.0 (3.0-8.0)**	5.0 (3.0-8.0)
Modic 1 vertebral endplate subchondral bone changes, n/N (%)			
L2-L3	4/67 (6.0)	3/68 (4.4)	7/135 (5.2)
L3-L4	3/67 (4.5)	7/68 (10.3)	10/135 (7.4)
L4-L5	24/67 (35.8)	21/68 (30.9)	45/135 (33.3)
L5-S1	37/67 (53.7)	37/68 (54.4)	73/135 (54.1)
Mean time elapsed between MRI and GC IDI (SD), d	69.7 (38.6)¶¶	80.6 (45.5)†††	75.1 (42.3)
Mean time elapsed between randomization and IDI (SD), d	40.0 (28.9)¶	41.2 (22.5)†††	40.6 (25.8)

CSQ = Coping Strategies Questionnaire; FABQ = Fear-Avoidance Beliefs Questionnaire; GC IDI = glucocorticoid intradiscal injection; HADS = Hospital Anxiety and Depression Scale; IQR = interquartile range; LBP = low back pain; MRI = magnetic resonance imaging; NRS = numerical rating scale; QBPDS = Quebec Back Pain Disability Scale; SF-12 = Study Short Form-12 Health Survey.

* 61 patients in the GC IDI group and 60 in the control group received the intervention. Percentages may not sum to 100 due to rounding.

† Higher scores indicate greater pain.

‡ n = 67.

§ Weak opioids include codeine, dihydrocodeine, and tramadol. Strong opioids include morphine, diamorphine, fentanyl, buprenorphine, oxycodone, and hydromorphone.

¶ Higher scores indicate more limitations.

¶¶ n = 61.

** n = 62.

†† Higher scores indicate better health.

‡‡ Higher scores indicate more clinically significant symptoms.

§§ Higher scores indicate greater fear and avoidance beliefs.

||| n = 58.

¶¶¶ n = 59.

*** Higher scores indicate more frequent use of coping skills.

††† n = 60.

Table 2. Percentage of Responders (LBP Intensity <40) at 1 Month After the Intervention (Primary Outcome)

Variable	Patients With LBP Intensity <40 in the Previous 48 h, n/N (%) [*]		Absolute Difference (95% CI), percentage points [§]	Relative Risk (95% CI)	P Value for Absolute Difference
	GC IDI Group (n = 67) [†]	Control Group (n = 68) [‡]			
Without imputation	36/65 (55.4)	21/63 (33.3)	22.0 (5.3–38.7)	1.66 (1.10–2.50)	–
After multiple imputation (mean of 20 imputations)	–	–	22.1 (5.5–38.7)	1.66 (1.11–2.50)	0.009

GC IDI = glucocorticoid intradiscal injection; LBP = low back pain.

^{*} On a numerical rating scale ranging from 1 to 100; higher scores indicate greater pain.

[†] 61 patients received the intervention.

[‡] 60 patients received the intervention.

[§] GC IDI group minus control group, adjusted for center.

^{||} GC IDI group vs. control group, adjusted for center.

RESULTS

Overall, 260 patients were screened, 153 were eligible, and 18 declined to participate. A total of 135 patients were randomly assigned to receive either a GC IDI during discography ($n = 67$) or discography alone ($n = 68$). Approximately 10% of randomly assigned patients did not receive the allocated intervention (Figure 1). The median age at inclusion was 46.0 years (range, 42.0 to 54.0 years), and women outnumbered men by a 2:1 ratio. Modic 1 changes were most frequently located at the L4-L5 (45 of 135 [33.3%]) or L5-S1 (73 of 135 [54.1%]) levels. The mean duration of the current LBP episode was 1.4 years (SD, 1.4) in the GC IDI group and 1.3 years (SD, 1.0) in the control group. Overall, 53 of 67 patients (79.1%) in the GC IDI group and 61 of 68 (89.7%) in the control group had a clinical phenotype consistent with active discopathy, with morning stiffness, nighttime awakenings, or both. The mean time between randomization and intervention was 40.0 days (SD, 28.9) in the GC IDI group and 41.2 days (SD, 22.5) in the control group, and the mean time between lumbar MRI and intervention was 69.7 (SD, 38.6) and 80.6 (SD, 45.5) days, respectively (Table 1).

Primary Outcome

At 1 month after the intervention, the percentage of responders (LBP intensity <40) was higher in the GC IDI group (36 of 65 [55.4%]) than the control group (21 of 63 [33.3%]) (absolute risk difference, 22.1 percentage points [CI, 5.5 to 38.7 percentage points]; $P = 0.009$ [after multiple imputation]) (Table 2). The percentage of responders per site is shown in Appendix Table 6 (available at Annals.org). In the sensitivity analysis, the mean reduction in LBP intensity from baseline to 1 month was greater in the GC IDI group (-32.5 [CI, -38.2 to -26.8]) than the control group (-17.5 [CI, -23.3 to -11.7]) (absolute difference, -15.0 [CI, -22.9 to -7.1]; $P < 0.001$).

Secondary Outcomes

At 1 month after the intervention, the percentage of patients reporting improvement in LBP-related limitations in activities was higher in the GC IDI group (55 of 65 [84.6%]) than the control group (34 of 63 [54.0%]) (absolute risk difference, 30.5 percentage points [CI, 15.7 to 45.2 percentage points]; $P < 0.001$), and no differences were seen at 12 months. Starting at 3 months,

pain scores increased in the GC IDI group and were higher than in the control group (Figure 2); and at 12 months, the 2 groups did not differ in LBP intensity (Table 3). At 12 months, the mean reduction from baseline in the HADS depression score was lower in the GC IDI group (-0.1 [CI, -1.2 to 1.0]) than in the control group (-1.7 [CI, -2.7 to -0.6]) (absolute difference, 1.6 [CI, 0.1 to 3.0]; $P = 0.035$). The groups did not differ in employment status at 12 months or in other secondary outcomes at 1 and 12 months (Table 3). Patients rated the predicted usefulness of the intervention in reducing their symptoms at 6.9 (SD, 1.9) on a scale of 1 (not useful) to 9 (very useful) (Appendix Table 4).

Tolerability and Acceptability of the Intervention

The median LBP intensity was 70.0 (interquartile range, 40.0 to 80.0) during the intervention, and 56 of 120 patients (46.7%) reported increased LBP after the intervention. The median score for acceptability was 6.0 (interquartile range, 4.0 to 8.0), and 102 of 119 (85.7%) patients would have agreed to a second intervention (Appendix Table 3).

Safety

At 12 months, 65 of 67 (97.0%) patients in the GC IDI group and 64 of 68 (94.1%) in the control group reported at least 1 adverse event (Appendix Table 5). A total of 78 serious adverse events were reported in both groups, including hospitalizations for usual care of chronic LBP (25 in the GC IDI group and 29 in the control group), hospitalizations for events unrelated to chronic LBP (14 in the GC IDI group and 5 in the control group), events unrelated to chronic LBP without hospitalization (3 in the GC IDI group and 1 in the control group), and 1 event possibly related to the intervention in the control group (increase in sciatica pain in the 24 hours after the intervention). One death (by suicide) was recorded in the GC IDI group. No infectious spondylodiscitis or intervertebral disc calcifications were observed (Appendix Table 5).

DISCUSSION

In this multicenter randomized trial of GC IDI in patients with chronic LBP associated with active discopathy, the percentage of responders (LBP intensity <40) at 1 month was higher in the GC IDI group in than the

control group. Starting at 3 months, pain scores increased in the GC IDI group and were higher than in the control group. At 12 months, the groups did not differ in pain intensity or most other secondary outcomes.

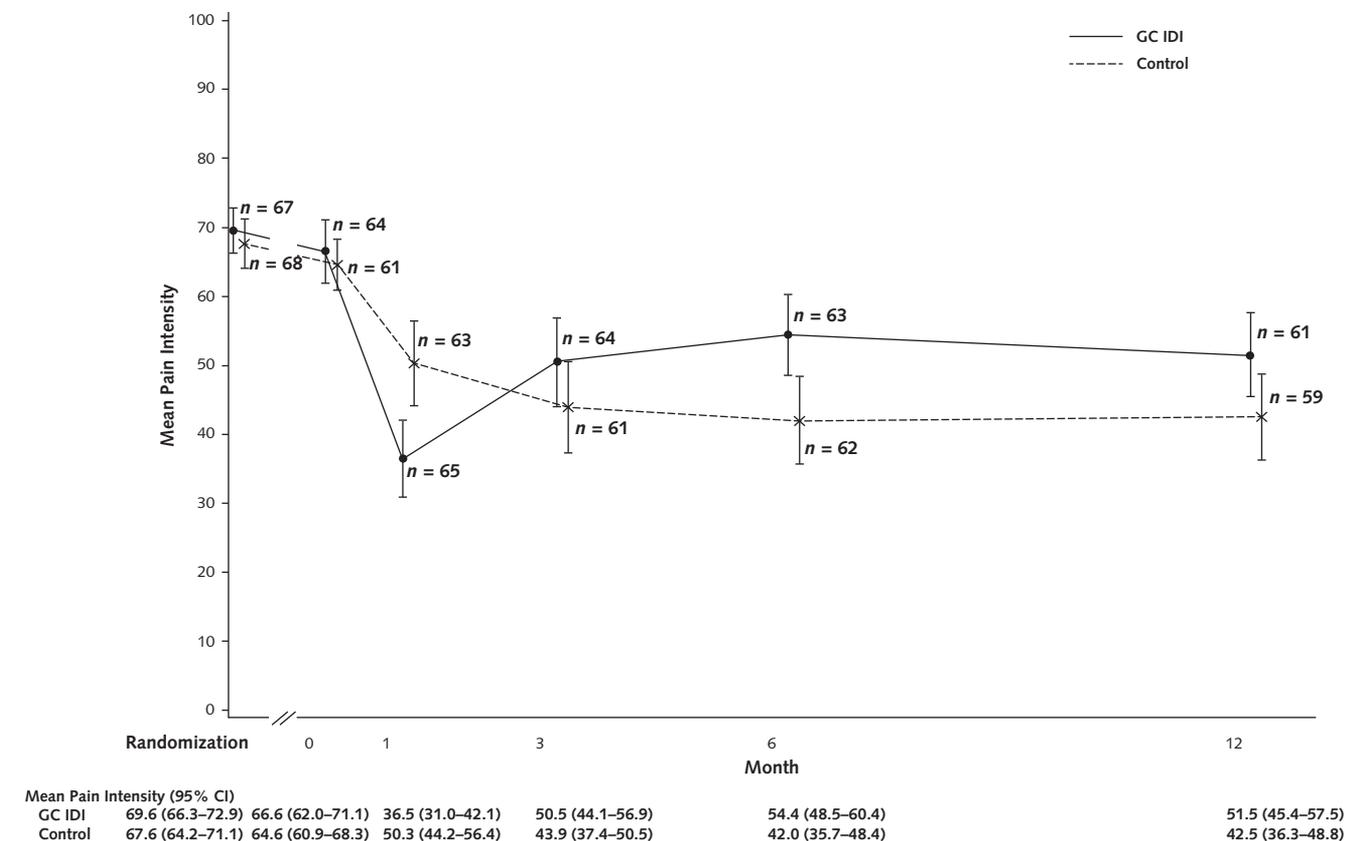
Overall, the intervention was considered acceptable. We found no cases of rapidly destructive disc disease (25) or intervertebral disc calcifications. Clinical and experimental data have raised concerns about possible harms of intradiscal procedures (26, 27) and toxicity of glucocorticoid on nucleus pulposus cells (28). In the late 1980s, GC IDI was even abandoned in France because of cases of compressive discal and peridural calcifications (29). The use of more soluble injectable glucocorticoid has prevented this complication (18).

Previous studies assessing GC IDI found results consistent with ours, but methodological concerns were raised with regard to their design and small sample size (15–18). In the present study, the rapid efficacy of GC IDI supports the role of local inflammation in the pathogenesis of symptoms related to active discopathy. Intradiscal injection with other anti-inflammatory agents, such as tumor necrosis factor- α and interleukin-6 blockers (30–32), has been assessed, but these agents were administered with other potent ac-

tive agents, such as anesthetics (20, 30–32). Therefore, immediate to short-term effects could not be attributed solely to the anti-inflammatory agents. Recently, the role of local inflammation has been challenged by the results of a randomized, placebo-controlled trial of 162 patients with chronic LBP associated with active discopathy, showing that treatment with antibiotics (amoxicillin-clavulanic acid for 100 days) was effective at 100 days and at 1 year (33). These findings suggested that local low-grade infection could occur in patients with active discopathy (33), but this hypothesis remains controversial (34). In the absence of antibiotic prophylaxis, we did not observe MRI findings consistent with infectious spondylodiscitis occurring at the level of the IDI at 12 months.

Several hypotheses could explain our results. The increase in pain starting at 3 months could be related to a rebound effect of glucocorticoids. Furthermore, our population had a severe condition, with a low employment rate, symptoms of depression and anxiety, fear-avoidance beliefs, and inappropriate coping strategies, which could have altered the treatment effect. Some researchers have suggested that GC IDI should be offered only to patients with chronic LBP with few confounding factors (35).

Figure 2. Mean lumbar pain intensity in previous 48 h, by intervention group.



Pain intensity was assessed on an 11-point numerical rating scale (0 [no pain] to 100 [maximum pain] in 10-point increments) at randomization; intervention (month 0); and 1, 3, 6, and 12 mo. Error bars represent 95% CIs. GC IDI = glucocorticoid intradiscal injection.

Table 3. Secondary Outcomes*

Outcome	GC IDI Group (n = 67)	Control Group (n = 68)	Absolute Difference (95% CI)†	Relative Risk (95% CI)‡	P Value for Absolute Difference
1 mo after intervention					
Mean change from baseline (95% CI)§					
QBPDS score (range, 0-100) ¶	-11.9 (-16.0 to -7.8)	-6.7 (-10.8 to -2.7)	-5.2 (-10.8 to 0.4)	-	0.069
SF-12 score (range, 0-100)**††					
Physical component	5.8 (3.5 to 8.0)	4.5 (2.2 to 6.8)	1.2 (-1.9 to 4.4)	-	0.44
Mental component	5.4 (3.0 to 7.9)	5.0 (2.5 to 7.5)	0.4 (-3.0 to 3.8)	-	0.81
HADS score (range, 0-21)‡‡					
Anxiety§§	-2.0 (-2.8 to -1.3)	-1.7 (-2.5 to -1.0)	-0.3 (-1.3 to 0.8)	-	0.58
Depression	-0.7 (-1.6 to 0.1)	-1.2 (-2.1 to -0.3)	0.5 (-0.7 to 1.6)	-	0.42
Full- or part-time employment, n/N (%)	39/65 (60.0)	40/63 (63.5)	-3.5 (-20.4 to 13.4)	0.94 (0.72 to 1.24)	0.69
Analgesics in the previous week, n/N (%)	42/64 (65.6)	47/63 (74.6)	-8.9 (-24.7 to 7.0)	0.88 (0.70 to 1.11)	0.27
Nonsteroidal anti-inflammatory drugs in the previous week, n/N (%)	14/63 (22.2)	19/63 (30.2)	-8.2 (-23.5 to 7.1)	0.73 (0.40 to 1.33)	0.29
Improvement in LBP-related limitations in activities, n/N (%)	55/65 (84.6)	34/63 (54.0)	30.5 (15.7 to 45.2)	1.56 (1.22 to 2.00)	<0.001
12 mo after intervention					
Mean change from baseline (95% CI)§					
LBP intensity on NRS (range, 0-100) ¶¶	-18.2 (-24.2 to -12.2)	-24.8 (-30.9 to -18.7)	6.6 (-1.8 to 15.0)	-	0.122
QBPDS score (range, 0-100) ***	-6.9 (-11.6 to -2.2)	-7.6 (-12.4 to -2.8)	0.7 (-5.8 to 7.3)	-	0.83
SF-12 score (range, 0-100)**					
Physical component†††	3.9 (1.7 to 6.1)	6.9 (4.6 to 9.2)	-3.0 (-6.2 to 0.1)	-	0.061
Mental component†††	2.9 (-0.1 to 5.9)	4.5 (1.4 to 7.6)	-1.6 (-5.8 to 2.6)	-	0.45
HADS score (range, 0-21)‡‡					
Anxiety‡‡‡	-1.6 (-2.5 to -0.8)	-1.9 (-2.8 to -1.1)	0.3 (-0.9 to 1.4)	-	0.63
Depression§§§	-0.1 (-1.2 to 1.0)	-1.7 (-2.7 to -0.6)	1.6 (0.1 to 3.0)	-	0.035
Full- or part-time employment, n/N (%)	40/61 (65.6)	41/59 (69.5)	-4.2 (-20.9 to 12.5)	0.94 (0.73 to 1.20)	0.62
Analgesics in the previous week, n/N (%)	48/61 (78.7)	41/59 (69.5)	9.8 (-5.7 to 25.1)	1.14 (0.92 to 1.41)	0.22
Nonsteroidal anti-inflammatory drugs in the previous week, n/N (%)	20/60 (33.3)	30/59 (50.9)	-17.2 (-34.7 to 0.3)	0.66 (0.43 to 1.02)	0.054
Improvement in LBP-related limitations in activities, n/N (%)	38/60 (63.3)	35/59 (59.3)	3.3 (-14.1 to 20.7)	1.06 (0.79 to 1.40)	0.71
Persistent Modic 1 signal on MRI, n/N (%)	53/58 (91.4)	49/55 (88.9)	2.2 (-8.9 to 13.2)	1.02 (0.91 to 1.16)	0.70

GC IDI = glucocorticoid intradiscal injection; HADS = Hospital Anxiety and Depression Scale; LBP = low back pain; MRI = magnetic resonance imaging; NRS = numerical rating scale; QBPDS = Quebec Back Pain Disability Scale; SF-12 = Short Form-12 Health Survey.

* 61 patients in the GC IDI group and 60 in the control group received the intervention.

† GC IDI group minus control group. Differences in mean changes from baseline values adjusted for baseline value and center. Differences in percentages adjusted for center.

‡ GC IDI group vs. control group, adjusted for center.

§ Adjusted for baseline value and center.

|| Higher scores indicate more limitations.

¶ n = 61 in the GC IDI group and 62 in the control group.

** Higher scores indicate better health.

†† n = 62 in the GC IDI group and 59 in the control group.

‡‡ Higher scores indicate more clinically significant symptoms.

§§ n = 60 in the GC IDI group and 57 in the control group.

||| n = 63 in the GC IDI group and 62 in the control group.

¶¶ Higher scores indicate greater pain. n = 61 in the GC IDI group and 59 in the control group.

*** n = 60 in the GC IDI group and 56 in the control group.

††† n = 57 in the GC IDI group and 52 in the control group.

‡‡‡ n = 62 in the GC IDI group and 62 in the control group.

§§§ n = 50 in the GC IDI group and 57 in the control group.

Our study has limitations. The dose regimen and properties of the glucocorticoid may have affected outcomes, as suggested by the increase in pain and the inability of the treatment to reverse MRI changes at 12 months. A dose-optimization schedule or a less soluble glucocorticoid might be needed, but the risks and benefits of the procedure would need to be considered (20, 36). We did not use provocation discography to select the disc in which to administer the injection. Although the purpose of discography is to determine

whether increasing the intradiscal pressure elicits pain, this test is invasive and has a high percentage of false-positive results (up to 25%) (37, 38). The difference in the volume injected might also have affected outcomes. Because all of the discs in which the injection was administered were degenerated and IDI was performed without resistance, the effects observed at 1 month after the intervention were probably not solely attributable to differences in pressure during injection. The MRI was obtained at 12 months, and we were un-

able to assess whether the positive effects of GC IDI on pain at 1 month were associated with structural improvements, as previously reported (19). Finally, participants were recruited from tertiary care centers and may not have been representative of the general French chronic LBP population with active discopathy.

In this trial of patients with chronic LBP associated with active discopathy, for whom first-line conservative treatments had failed, patients who received a single GC IDI had positive effects on pain at 1 month compared with the control group. This effect decreased over time, with no differences in LBP intensity between groups at 12 months. The efficacy of GC IDI as a possible treatment for chronic LBP associated with active discopathy is questionable, given the lack of long-term benefit.

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Reproducible Research Statement: *Study protocol:* An English translation of the Methods section of the original study protocol and statistical analysis plan as well as a summary of changes are available in the **Supplement**. The full original French version of the protocol is available from Prof. Rannou (e-mail, francois.rannou@aphp.fr). *Statistical code:* Available from Dr. Baron (e-mail, gabriel.baron@aphp.fr). *Data set:* Available from Prof. Rannou (e-mail, francois.rannou@aphp.fr).

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Appendix Table 1. Important Changes to Methods After Trial Commencement and the Reasons for Those Changes

Changes in outcomes after trial commencement

"Leisure activity" was removed from secondary efficacy outcomes because we did not expect the treatment to modify "leisure activity" (Amendment no. 1, version 2.0, of 8/13/09). "Leisure activity" was not collected in any patient.

"Success of blinding" of the intervention assessed by the Credibility/Expectancy Questionnaire was added to safety outcomes in the protocol, although it should not be considered as an outcome but as an assessment of the quality of the methods used (Amendment no. 1, version 2.0, of 8/13/09). "Success of blinding" was collected in 119 of 121 patients receiving the intervention (60 of 61 in the glucocorticoid intradiscal injection group and 59 of 60 in the placebo group, respectively).

Change in definition: "Return to work" was prespecified and registered as a secondary efficacy outcome. However, the variable we collected and tested was actually "employment status" (in activity/sick leave/invalidism/retired/unemployed) and we did analyze the percentage of patients in activity.

Changes in eligibility or inclusion or exclusion criteria after trial commencement

Expansion of inclusion criterion regarding age from patients aged 60-65 y (inclusive). The aim of expanding the inclusion criterion regarding age was to be able to enroll more patients and therefore reach the number of patients initially set (Amendment no. 1, version 2.0, of 8/13/09).

Expansion of inclusion criterion regarding age from patients aged 65-70 y (inclusive). The aim of expanding the inclusion criterion regarding age was to be able to enroll more patients and therefore reach the number of patients initially set (Amendment no. 2, version 3.0, of 8/9/10).

1 inclusion criterion was added: "History of intradiscal injection at least 6 months before." The aim of adding this inclusion criterion was to increase the rate of enrollment and therefore reach the planned objectives. Persistence of pain and a Modic 1 signal indicate the persistence of a local inflammatory reaction, making the indication logical (Amendment no. 2, version 3.0, of 8/9/10).

The exclusion criterion "history of surgery" was made more specific: "History of surgery within the past 6 months." The aim of changing this exclusion criterion was to increase the rate of enrollment and therefore reach the initially planned objectives. The local inflammatory phenomena linked to the surgery disappear within the first 4 months. The persistence of a Modic 1 signal at 6 months evokes active disc disease, making the indication logical (Amendment no. 2, version 3.0, of 8/9/10).

Errors of registration on ClinicalTrials.gov

"Fears-avoidance belief" and "coping strategies" were registered by error as secondary efficacy outcomes on ClinicalTrials.gov. In the original (version 1.1, 5/20/08), successive, and final (version 5.0, 3/28/12) versions of the protocol, "fears-avoidance belief" and "coping strategies" were not listed as secondary outcomes. These variables were collected at baseline only. In fact, we did not expect the treatment to modify fears-avoidance belief and coping strategies. Changes on ClinicalTrials.gov on 5/6/15 were aimed to correct these errors in registration.

The safety outcomes were not properly registered in ClinicalTrials.gov. However, all the safety outcomes prespecified in the final version of the protocol (version 5.0, 3/28/12), namely, acceptability of the intervention, pain intensity and success of blinding during the intervention (although success of blinding should probably not be considered as an outcome), and loss of disc height (in millimeters and percentages) and intervertebral disc calcifications at 12 months after the intervention, have been reported in the present manuscript in sections 3 to 5 of the Supplement.

Errors in the description of the primary outcome in the original protocol

There is a discrepancy in the description of the primary end point between sections 9.1, 11.1, and 11.3 of the original protocol. Section 11.3 says the primary end point was mean change in low back pain at 1 month, but this was an error; the correct description of the primary end point is provided in the original protocol in section 9.1 ("The primary endpoint will be pain within the 48 hours before the consultation at 1 month after the intervention, as measured by a numeric pain scale from 0 to 100. The success rate expressed is defined by a pain assessment score lower than 40 out of 100 on a numeric pain scale over the past 48 hours . . .") and section 11.1 ("This number of subjects would allow us to show an absolute difference of 20%, i.e. 10% success in the control group and 30% success in the experimental group. Treatment success will be defined by a pain assessment score lower than 40 on a numeric pain scale over the past 48 hours . . .").

Appendix Table 2. Additional Inclusion and Exclusion Criteria

Inclusion criteria

Age 18-70 y
Lack of efficacy of usual recommended treatments: analgesics and nonsteroidal anti-inflammatory drugs
Lack of efficacy of other spinal steroid injections: epidural or facet joint
Intradiscal injection ≥ 6 mo before inclusion
Written informed consent
Social Security coverage
Medical examination

Exclusion criteria

Pregnancy
Hypersensitivity to prednisolone acetate or contrast agent
Local or general infection
Previous disc surgery or nucleolysis <6 mo
Current oral steroid treatment
Previous or ongoing infectious spondylodiscitis
Ankylosing spondylitis
Sciatica with neurologic defects
Uncontrolled psychiatric disorders
Anti-vitamin K treatments
Severe coagulation diseases
Fever (temperature >38 °C) or erythrocyte sedimentation rate after 1 h >20 mm
Discopathy with Modic 1 signal changes on several lumbar levels
Inability to read or understand French

Appendix Table 3. Tolerability and Acceptability of the Intervention and Technical Issues

Variable	GC IDI Group (n = 67)*	Control Group (n = 68)†	All Patients (n = 135)
Unspecified technical difficulties, n/N (%)	5/61 (8.2)	4/60 (6.7)	9/121 (7.4)
Proper needle positioning, n/N (%)	59/60 (98.3)	59/60 (98.3)	118/120 (98.3)
LBP provocation during intervention, n/N (%)	31/61 (50.8)	29/60 (48.3)	60/121 (49.6)
Median LBP intensity during the intervention on NRS (IQR) (range, 0-100)	70.0 (40.0-80.0)‡	70.0 (30.0-80.0)§	70.0 (40.0-80.0)
Localized bleeding during intervention, n/N (%)	0/61 (0)	0/60 (0)	0/121 (0)
LBP intensity increase after intervention, n/N (%)	27/61 (44.3)	29/59 (49.2)	56/120 (46.7)
Allergic reaction after intervention, n/N (%)	0/61 (0)	0/59 (0)	0/120 (0)
Vagal adverse reaction after intervention, n/N (%)	3/61 (4.9)	6/59 (10.2)	9/120 (7.5)
Median acceptability of the intervention on NRS (IQR) (range, 0-10)	6.0 (5.0-8.0)§	6.0 (4.0-8.0)§	6.0 (4.0-8.0)
Would agree to a second intervention, n/N (%)	53/60 (88.3)	49/59 (83.1)	102/119 (85.7)

GC IDI = glucocorticoid intradiscal injection; IQR = interquartile range; LBP = low back pain; NRS = numerical rating scale.

* 61 patients received the intervention.

† 60 patients received the intervention.

‡ n = 60.

§ n = 59.

Appendix Table 4. Success of Blinding Assessed by the Credibility/Expectancy Questionnaire at the Time of Intervention*

Question	GC IDI Group (n = 67)†	Control Group (n = 68)‡	All Patients (n = 135)
At this point, how logical does the group therapy offered to you seem? (1 [not logical] to 9 [very logical])	6.9 (1.9)§	7.4 (1.7)	7.2 (1.8)
At this point, how useful do you think this treatment will be in reducing your symptoms? (1 [not useful] to 9 [very useful])	6.8 (2.0)	7.1 (1.8)	6.9 (1.9)
How confident would you be in recommending this treatment to a friend who experiences similar problems? (1 [not confident] to 9 [very confident])	6.7 (2.1)§	7.1 (2.0)	6.9 (2.0)
By the end of the therapy period, how much improvement in your symptoms do you think will occur? (1 [no improvement] to 9 [total improvement])	7.2 (1.8)§	7.6 (1.4)	7.4 (1.6)
At this point, how much do you really feel that therapy will help you to reduce your symptoms? (1 [not at all] to 9 [totally])	6.6 (2.0)§	6.8 (1.9)	6.7 (1.9)
By the end of the therapy period, how much do you really feel that therapy will help you to improve your symptoms? (1 [not at all] to 9 [totally])	6.7 (1.9)§	6.7 (1.8)	6.7 (1.8)

GC IDI = glucocorticoid intradiscal injection.

* Values are means (SDs).

† 61 patients received the intervention.

‡ 60 patients received the intervention.

§ n = 60.

|| n = 59.

Appendix Table 5. Safety Profile During 12-Month Follow-up*

Variable	GC IDI Group (n = 67)	Control Group (n = 68)	All Patients (n = 135)
≥1 adverse event, n/N (%)	65/67 (97.0)	64/68 (94.1)	129/135 (95.6)
≥1 serious adverse event, n/N (%)	29/67 (43.3)	27/68 (39.7)	56/135 (41.5)
Median total adverse events (IQR), n	5.0 (4.0 to 6.0)†	5.0 (3.0 to 7.0)‡	5.0 (3.0 to 6.0)
Median total serious adverse events (IQR), n	1.0 (1.0 to 2.0)§	1.0 (1.0 to 1.0)	1.0 (1.0 to 2.0)
Adverse events time frame after treatment, n/N (%)			
Before 1 mo	37/63 (58.7)	47/63 (74.6)	84/126 (66.7)
1-3 mo	44/64 (68.8)	35/61 (57.4)	79/125 (63.2)
3-6 mo	47/63 (74.6)	32/60 (53.3)	79/123 (64.2)
6-12 mo	52/61 (85.2)	45/59 (76.3)	97/120 (80.8)
Types of adverse events			
Lumbar surgery during follow-up, n/N (%)	5/67 (7.4)	0/68 (0)	5/135 (3.7)
Intervertebral disc calcification, n/N (%)	0/58 (0)	0/53 (0)	0/111 (0)
Infectious spondylodiscitis, n/N (%)	0/58 (0)	0/53 (0)	0/111 (0)
Loss of disc height			
Median anterior (IQR)			
Millimeters	-1.2 (-2.7 to 0.6)¶	-0.8 (-3.0 to 0.3)**	-0.9 (-2.7 to -0.5)
Percentage	-9.3 (-18.8 to 4.4)¶	-5.4 (-15.2 to 1.9)**	-8.0 (-18.4 to 4.1)
Median posterior (IQR)			
Millimeters	-0.4 (-2.1 to 1.1)††	-0.7 (-2.4 to 0.3)‡‡	-0.5 (-2.3 to 0.7)
Percentage	-5.9 (-24.2 to 16.2)††	-8.1 (-35.9 to 4.0)‡‡	-7.1 (-30.8 to 10.1)
Median medial (IQR)			
Millimeters	-0.5 (-1.5 to 0.3)§§	-0.5 (-1.9 to 0.6)	-0.5 (-1.6 to 0.6)
Percentage	-3.9 (-16.9 to 2.6)§§	-5.7 (-19.1 to 7.3)	-5.0 (-17.9 to 5.3)
Types of serious adverse events, n/N (%)			
Hospitalizations for usual care of chronic LBP¶¶	21/67 (31.3)	23/68 (33.8)	44/135 (32.6)
Hospitalizations for events unrelated to chronic LBP***	11/67 (16.5)	5/68 (7.4)	16/135 (11.9)
Events related to chronic LBP without hospitalization	0/67 (0)	0/68 (0)	0/135 (0)
Events unrelated to chronic LBP without hospitalization†††	2/67 (3.0)	1/68 (1.5)	3/135 (2.2)
Event possibly related to the intervention	0/67 (0)	1/68 (1.5)	1/135 (0.7)
Deaths, n/N (%)	1/67 (1.5)	0/68 (0)	1/135 (0.7)

GC IDI = glucocorticoid intradiscal injection; IQR = interquartile range; LBP = low back pain.

* 61 patients in the GC IDI group and 60 in the control group received the intervention. Adverse events were defined as any untoward medical occurrence that did not necessarily have a causal relationship with the clinical trial or the experimental product. Serious adverse events were defined as any untoward medical occurrence that resulted in death, were life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, or resulted in persistent or clinically significant disability.

† n = 65.

‡ n = 64.

§ n = 29.

|| n = 27.

¶ n = 39.

** n = 37.

†† n = 44.

‡‡ n = 36.

§§ n = 42.

||| n = 40.

¶¶ 54 hospitalizations occurred and affected a total of 44 of 135 patients: 10 patients (6 in the GC IDI group and 4 in the control group) had 2 events, and 34 patients (15 in the GC IDI group and 19 in the control group) had 1 event.

*** 19 hospitalizations occurred and affected a total of 16 of 135 patients: 3 patients the GC IDI group had 2 events, and 13 patients (8 in the GC IDI group and 5 in the control group) had 1 event.

††† 4 events occurred and affected a total of 3 of 135 patients: 1 patient in the GC IDI group had 2 events, and 2 patients (1 in the GC IDI group and 1 in the control group) had 1 event.

Appendix Table 6. Percentage of Responders (LBP Intensity <40) at 1 Month After the Intervention (Primary Outcome), by Site

Hospital	Patients With LBP Intensity <40 in the Previous 48 h, n/N (%)*		
	GC IDI Group (n = 67)†	Control Group (n = 68)‡	All Patients (n = 135)
Cochin Hospital§	32/58 (55.2)	20/57 (35.1)	52/115 (45.2)
Lariboisière Hospital	4/7 (57.1)	1/9 (11.1)	5/16 (31.3)
Lille Hospital¶	0/2 (0)	0/2 (0)	0/4 (0)

GC IDI = glucocorticoid intradiscal injection; LBP = low back pain.

* On a numerical rating scale ranging from 1 to 100.

† 61 patients received the intervention.

‡ 60 patients received the intervention.

§ 11 of 115 patients (9.6%) did not receive the intervention: 5 of 58 (8.6%) in the GC IDI group and 6 of 57 (10.5%) in the control group.

|| 3 of 16 patients (18.8%) did not receive the intervention: 1 of 7 (14.3%) in the GC IDI group and 2 of 9 (22.2%) in the control group.

¶ All 4 patients received the intervention.