The protein hormone leptin, encoded by the obese gene and produced by adipose tissue,1-6 appears to signal adiposity and modulate ingestive behavior. Several lines of evidence support this conclusion: exogenous leptin administration results in a loss of body fat in ani-

**Context** The protein hormone leptin is important to the homeostatic regulation of body weight. Treatment with exogenous leptin may affect weight loss.

**Objective** To determine the relationship between increasing doses of exogenous leptin administration and weight loss in both lean and obese adults.

**Design** A randomized, double-blind, placebo-controlled, multicenter, escalating dose cohort trial conducted from April 1997 to October 1998.

**Setting** Four university nutrition and obesity clinics and 2 contract clinical research clinics.

**Participants** Fifty-four lean (body mass index, 20.0-27.5 kg/m^2^; mean [SD] body weight, 72.0 [9.7] kg) and 73 obese (body mass index, 27.6-36.0 kg/m^2^; mean [SD] body weight, 89.8 [11.4] kg) predominantly white (80%) men (n = 67) and women (n = 60) with mean (SD) age of 39 (10.3) years.

**Interventions** Recombinant methionyl human leptin self-administered by daily morning subcutaneous injection (0 [placebo], 0.01, 0.03, 0.10, or 0.30 mg/kg). In part A, lean and obese subjects were treated for 4 weeks; in part B, obese subjects were treated for an additional 20 weeks. Lean subjects consumed a eucaloric diet to maintain body weight at the current value, and obese subjects were prescribed a diet that reduced their daily energy intake by 2100 kJ/d (500-kcal/d) from the amount needed to maintain a stable weight.

**Main Outcome Measures** Body weight, body fat, and incidence of adverse events.

**Results** Weight loss from baseline increased with increasing dose of leptin among all subjects at 4 weeks (P = .02) and among obese subjects at 24 weeks (P = .01) of treatment. Mean (SD) weight changes at 4 weeks ranged from −0.4 (2.0) kg for placebo (n = 36) to −1.9 kg (1.6) kg for the 0.1 mg/kg dose (n = 29). Mean (SD) weight changes at 24 weeks ranged from −0.7 (5.4) kg for the 0.01 mg/kg dose (n = 6) to −7.1 (8.5) kg for the 0.30 mg/kg dose (n = 8). Fat mass declined from baseline as dose increased among all subjects at 4 weeks (P = .002) and among obese subjects at 24 weeks of treatment (P = .004); more than 95% of weight loss was fat loss in the 2 highest dose cohorts at 24 weeks. Baseline serum leptin concentrations were not related to weight loss at week 4 (P = .88) or at week 24 (P = .76). No clinically significant adverse effects were observed on major organ systems. Mild-to-moderate reactions at the injection site were the most commonly reported adverse effects.

**Conclusions** A dose-response relationship with weight and fat loss was observed with subcutaneous recombinant leptin injections in both lean and obese subjects. Based on this study, administration of exogenous leptin appears to induce weight loss in some obese subjects with elevated endogenous serum leptin concentrations. Additional research into the potential role for leptin and related hormones in the treatment of human obesity is warranted.

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mals, animals and humans who have a genetic deficiency of leptin exhibit extreme obesity; and serum concentrations of leptin increase with body fat in very obese persons who do not have a genetic mutation. Leptin levels and body fat are highly correlated, and body fat accounts for approximately 50% to 60% of the variation in serum leptin concentrations among people. Other factors (eg, sex, diurnal variation, and serum insulin concentration) correlate to a lesser extent.

Leptin concentrations in the cerebrospinal fluid (CSF) increase with body fat but are generally 2 orders of magnitude lower than serum concentrations. The ratio of CSF to serum leptin concentrations also appears to be lower in obese subjects. These relationships suggest that administering exogenous leptin might affect homeostatic mechanisms of energy regulation to alter body weight. Alternatively, the higher serum leptin concentrations in obese subjects may suggest that exogenous leptin administration would be ineffective in decreasing adiposity.

We report herein the effects of an exogenously administered recombinant leptin, studied in a randomized, double-blind, placebo-controlled, escalating-dose cohort trial in lean and obese adult subjects. The hypothesis was tested that increasing doses of exogenous leptin administration would result in dose-dependent weight loss in both lean and obese adults.

**METHODS**

**Study Design**

The study was conducted from April 1997 to October 1998 at 4 university nutrition and obesity clinics and 2 contract clinical research clinics. Subjects enrolled at the university clinics were selected from the investigators’ patient populations; subjects at the contract clinical research clinics were selected from their client databases. The hypothesis was tested by monitoring body weight and composition changes among subjects randomly assigned to escalating dose groups of recombinant methionyl human leptin (rL) (Amgen Inc, Thousand Oaks, Calif) or matching placebo (sorbitol and sodium acetate, pH 4.0). Subcutaneous bolus injections (0.01, 0.03, 0.10, or 0.30 mg/kg per day or placebo) were prescribed to 2 strata of lean subjects whose body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters, was 20.0 to 23.4 kg/m² and 23.5 to 27.5 kg/m² and to 2 strata of overweight and obese subjects whose BMI was 27.6 to 30.0 kg/m² and 30.1 to 36.0 kg/m², respectively. For simplicity, the latter 2 cohorts are collectively referred to as obese. Subjects were healthy lean and obese adults. Those with comorbidities of obesity, especially drug-treated diabetes, hyperlipidemia, and hypertension, were excluded. Women were postmenopausal or surgically sterile. All subjects provided written informed consent. An investigational review board at each study site approved the protocol.

As part of the dose escalation, some subjects received rL by subcutaneous continuous infusion at dosages of up to 2 mg/kg per day, which produced entirely different pharmacokinetics. This report summarizes results of subjects given bolus injections. One group of subjects treated with 0.3 mg/kg per day of rL provided at a higher concentration experienced unacceptable reactions at the injection site (eg, ecchymosis, erythema, pruritus), referred to collectively as injection site reactions (ISRs). Enrollment in this group was halted by the data monitoring committee after 11 subjects were treated for 4 weeks or less. The study drug was discontinued, and the results from these subjects are not included.

This study was conducted in 2 parts. Dose response to rL was evaluated in both lean and obese subjects for 4 weeks (part A). Because the effects of rL were unknown and prolonged weight loss was not desirable in lean subjects, only obese subjects were allowed to continue for an additional 20 weeks (part B). Lean subjects in part A were maintained on a eu- caloric diet, a diet that maintains body weight at the current value, and obese subjects in parts A and B were prescribed a diet that reduced their daily energy intake by 2100 kJ/d (500 kcal/d) from the amount needed to maintain a stable weight with nutritional counseling; 3-day food intake diaries were used to monitor subject adherence to the diet. Obese subjects were encouraged to walk briskly for 20 to 30 minutes, 3 to 5 times per week. Blinded study drug (placebo and rL) was self-administered subcutaneously once daily before 11 AM. Compliance was assessed by accounting for vials of study drug used.

**End Points and Measures**

Body weight, measured to the nearest 0.1 kg on calibrated scales, was the primary end point. Body composition (weight, fat mass, and fat-free mass) was determined by dual x-ray absorptiometry (DXA) using Lunar DPX densitometers (Lunar Corporation, Madison, Wis). All sites used the same model densitometers, software, and scan mode. DXA systems were calibrated, and scans were analyzed by a central reading laboratory (Bone Fide Ltd, Madison, Wis). To control for hydration status, subjects were instructed not to eat or drink anything other than small amounts of water for at least 8 hours prior to the scan and to avoid strenuous exercise or ingestion of alcohol in the 24 hours prior to the scan.

A central service (Professional Nutrition Systems, Westwood, Kan) estimated energy intake from subjects’ food diaries of the 48 hours before a clinic visit. Fasting glucose and insulin concentrations were measured periodically throughout the study. An oral glucose tolerance test (OGTT) (75 g of glucose) was performed at baseline and at the end of parts A (4 weeks) and B (24 weeks). Clinical safety and tolerability evaluations done throughout the study included performing physical examinations and electrocardiograms; checking for adverse events; and measuring serum chemistries, complete blood cell counts, hormone levels (luteinizing hormone, follicle-stimulating hormone, cortisol, and prolactin), and vital signs. In this multicenter trial, clinical chemistry analyses were conducted at a College of American Pathologists–certified...
central laboratory (MRL Medical Research Laboratory, Highland Heights, Ky). Serum leptin concentrations were determined by an enzyme-linked immunosorbent assay with a detection limit of 0.04 ng/mL; the assay does not distinguish between endogenous leptin and rL. The presence of serum antibodies against rL was assessed using a solid-phase radioimmunoassay using protein A tagged with iodine 125 to detect IgG bound to rL. Injection site reactions were graded as mild (easily tolerated), moderate (some discomfort), or severe (severe discomfort).

**Statistical Methods**

This study was designed to assess safety and to assess dose-response relationships. At each dose, subjects across all BMI groups were pooled to assess safety. After 8 subjects who were taking the study drug had completed 2 weeks of treatment, the study’s safety monitoring committee—1 scientist, 2 physicians, and 2 statisticians—reviewed the clinical data. In the absence of any unexpected or clinically significant findings, subject enrollment in the next dose cohort was permitted. After the safety assessment, a 6-subject cohort (4 active and 2 placebo) within each BMI strata was evaluated for weight loss at 2 weeks. If the weight loss difference between active and placebo was less than 0.5 kg or greater than 1.5 kg, no additional subjects were to be enrolled in that dose group. If weight loss effects were between these limits, an additional 6-subject cohort could be enrolled to further characterize weight loss. The operating characteristics of this design ensured an adverse event incidence of at least 30% would be detected with 95% probability. Simulations indicate that this design has at least 80% power to detect a true difference in weight loss of 1.0 kg between active and placebo groups.

All randomly assigned subjects who received at least 1 dose of the study medication were included in these analyses. The primary analysis included data for all subjects with measurements at each time point. As a means of evaluating the robustness of the analysis, a secondary analysis used the last observation carried forward method to impute data for subjects who withdrew prematurely. Results are expressed as mean (SD), unless otherwise noted.

Dose-response relationships were established by simple linear regression methods. The statistical assumptions for regression analyses were met. Subjects in the placebo group were pooled for analysis and assigned a dose of 0. Inferential analyses were assessed at the $P = .05$ significance level. Unplanned multiple comparisons against the placebo group were adjusted using Dunnett’s method. Statistical software SAS version 6.12 and JMP version 3.2.2 (SAS Institute, Cary, NC) were used to perform the analyses.

**RESULTS**

**Subject Characteristics and Disposition**

Of the 274 subjects assessed for inclusion in the study, 147 were ineligible (FIGURE 1). The subject pool at randomization consisted of 127 subjects. The mean (SD) body weight of the 54 lean subjects was 72.0 (9.7) kg and was 89.8 (11.4) kg for the 73 obese subjects. (TABLE 1). At baseline, subject

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**Figure 1. Subject Disposition in 2 Study Phases**

The 2-part study included lean and obese subjects. Lean subjects were treated with a weight maintaining diet and obese subjects were treated with a reduced-energy diet. Both groups received either placebo or recombinant methionyl human leptin (rL) for 4 weeks (part A). The second part of the study included only obese subjects who were similarly treated for 20 weeks (part B). Each weight category includes 2 weight ranges (see “Methods” section). The asterisk indicates a subject in the 0.1-mg/kg per day dose group who withdrew because of injection site reactions. The dagger indicates a subject in the 0.1-mg/kg dose group who had heart palpitations that were considered unlikely to be related to rL treatment. The double dagger indicates subject withdrew from the 0.01-mg/kg per day dose group because of injection site reactions.
characteristics were comparable between lean and obese subjects (except body weight) and among dose cohorts (Table 1). The distribution of body weights were balanced within each dose cohort. Sixty of the 70 obese subjects who completed part A continued into part B (Figure 1 and TABLE 2). Eight of the 10 obese subjects who chose not to continue in part B had been enrolled in the 0.3-mg/kg dose cohort (1 placebo-treated, 7 rL-treated) and received the highest injection volumes. Seven of the 9 obese subjects in the placebo group who dropped out did so in part B.

### Weight Loss and Body Composition

At the conclusion of part A (4 weeks' treatment), absolute weight changes across the doses studied averaged between −0.4 and −1.9 kg (mean [SD] weight change: placebo [n = 36], −0.4 [2.0] kg; 0.30-mg/kg rL dose, [n = 26], 1.5 [2.0] kg; Figure 2). At the conclusion of part B (24 weeks' treatment), absolute weight changes across the doses studied averaged between −0.7 and −7.1 kg with greatest average weight loss in the highest dose cohort (mean [SD] weight change: placebo [n = 12], −1.3 [4.9] kg; 0.30-mg/kg rL dose, [n = 8], −7.1 [8.5] kg; Figure 2).

There were statistically significant dose responses for weight loss from baseline among those who completed 4 weeks of treatment (53 lean and 70 obese subjects, \(P = .02\)) and 24 weeks of treatment (47 obese subjects, \(P = .01\), Figure 3). The relationship between escalating dose and weight loss was corroborated using a last observation carried forward analysis (TABLE 3). There was a statistically significant difference in weight loss across doses between lean and obese subjects at 4 weeks (\(P = .03\); lean subjects lost about the same amount of weight at all doses. There was no statistically significant relationship between baseline serum leptin concentrations and weight loss at week 4 (\(P = .88\)) or at week 24 (\(P = .76\)).

Body composition changes, as quantified by DXA, are presented in Figure 4. Decreases in fat mass showed statistically significant dose responses at 4 weeks and at 24 weeks (Figure 4, top). The loss in fat mass accounted for more than 95% of the weight loss in the 2 highest-dose cohorts at 24 weeks. Changes in fat-free mass were not significant (Figure 4, bottom).

There was no statistically significant relationship between change in energy intake and dose at week 4 (\(P = .87\)) or at week 24 (\(P = .36\)); average (SD) energy intake deficit across all dose groups was 1596 (3788) kcal/d (380 [902] kcal/d) at week 4 and 1819 (3767) kcal/d (433 [897] kcal/d) at week 24. Obese subjects treated with 0.1 and 0.3 mg/kg of rL had lower mean (SD) energy intake than subjects treated with placebo at week 4 (76 [19.7] kcal/kg per day [18.1

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[4.7 kcal/kg per day] [n = 25] vs 100 [61.7] kJ/kg per day [23.8 [14.7] kcal/kg per day] [n = 11], respectively, and at week 24 (85.3 [20.2] kJ/kg per day [20.3] [4.8] kcal/kg per day] [n = 20] vs 101.6 [18.5] kJ/kg per day [24.2 [4.4] kcal/kg per day] [n = 6], respectively) (P = .09 for both comparisons).

Safety Measures
Injection site reactions mild (86%) to moderate (14%) in severity were the most common adverse events are reported and summarized in Table 4. Injection site reactions were generally well tolerated by most subjects; 2 subjects withdrew because of them (Figure 1). For obese subjects who experienced injection site erythema, pruritus, or inflammation (considered characteristic of subcutaneous administration of a protein), the mean (SD) number of such events per subject was 1.7 (0.6), placebo; 3.0 (2.4), 0.01 dose; 3.5 (3.5), 0.03 dose; 27.5 (32.9), 1.0 dose; and 41.6 (57.8), 0.3 mg/kg per day cohorts over the 24-week course of the study.

The next most common adverse event was headache, which occurred in 38% and 44% of the placebo- and rL-treated subjects, respectively. None of the subjects taking rL experienced clinically significant adverse effects on major organ systems (central nervous system, cardiovascular, hepatic, renal, gastrointestinal, hematologic) as evidenced by adverse event incidence, physical examinations, laboratory values, electrocardiograms, and vital signs. There were no effects of rL on glycemic control or insulin action, as evidenced by serum insulin and glucose profiles obtained during OGTTs. There were no clinically or statistically significant treatment effects on serum concentrations of luteinizing hormone, follicle-stimulating hormone, cortisol, or prolactin.

Pharmacokinetics and Antibodies to rL
Maximum serum concentrations of leptin (endogenous leptin plus rL) increased with dose (Table 5). Pharmacokinetic analysis demonstrated that serum concentrations of rL peaked approximately 4 hours after injection.21 Among subjects from data were available, 32 (38%) of 85 in the 4-week cohort receiving subcutaneous doses and 25 (71%) of 35 in the 24-week cohort tested positive for antileptin antibodies. A statistically significant increasing proportion of subjects were positive for antileptin antibodies with increasing dose (trend test, P < .01 and P < .001 at 4 and 24 weeks, respectively). Antibody status (positive or negative for the presence of antileptin antibodies) had no statistically significant independent effect on weight loss at 4 weeks (P = .77) or at 24 weeks (P = .12) after accounting for the effects of treatment and dose cohort on weight loss. At 4 weeks, there was no association of the occurrence of adverse events (P = .11) or ISRs (P = .13) with antibody status. By 24 weeks, all subjects had experienced at least 1 adverse event; thus, an association between the overall incidence of adverse events and antibody status could not be determined. There was an association of the occurrence of ISRs (P = .008)
with antibody status at 24 weeks: 16 (64%) of 25 antibody-positive subjects experienced ISRs, while 5 (23%) of 22 antibody-negative subjects experienced ISRs.

**COMMENT**

These data show that a dose-response relationship exists both after 4 weeks of exposure to recombinant leptin in lean and obese subjects and after 24 weeks of exposure in obese subjects. There was considerable variability in the amount of weight lost by individual subjects; on average, weight loss increased with rL dose. Weight loss in subjects treated with rL was primarily due to fat loss, which accounted for more than 95% of the weight lost among obese subjects in the 2 highest-dosing cohorts after 24 weeks.

These findings do not suggest an absolute leptin resistance in obese individuals with elevated endogenous leptin levels; however, there still may be relative leptin resistance with increasing adiposity. Higher doses of exogenous leptin may be required to provide a sufficient signal for weight loss in subjects with greater adiposity.

We presume that weight loss is related to increased central nervous system exposure to exogenous leptin. In a separate substudy in a group of subjects treated with rL by continuous subcutaneous infusion, CSF leptin concentrations were elevated by exogenous subcutaneous leptin administration. Direct central nervous system administration of rL also induces weight loss in animals. These observations are consistent with the hypothesis that the effects of rL on weight are centrally mediated.

The therapeutic potential for rL to treat obesity cannot be determined from the results of this study. Although statistically significant dose-response relationships for weight loss and fat loss were observed in this study, differences between dose groups were not detectable given the study design.

Two children with genetic leptin deficiency have been reported; 1 has been treated with rL and has shown substantial weight loss with a low dose, demonstrating the biologic activity of rL. Three consanguineous people have been found to have very high serum leptin concentrations and a defect in the leptin receptor and would be predicted not to respond to exogenous administration of rL.

As part of the routine dietary intervention in our study, obese subjects were prescribed a 2100-kJ (500-kcal) deficit diet that, if followed, would lead to an average weight loss of 0.5 kg/wk. Placebo-treated obese subjects lost an average of 1.7 kg in 24 weeks; thus, long-term dietary compliance was poor in these subjects. The actual effect of the dietary intervention was therefore minimal in this study. Lower energy intake

| Table 3. Comparison of Observed and Imputed Weight Loss Results in Obese Subjects From Baseline to Week 24* |
|-----------------|-----------------|-----------------|
| **rL Dosage,** | **Mean (SD) Weight Change From Baseline, kg** | **No. of Subjects** | **Observed Value** | **No. of Subjects** | **Imputed Value** |
| mg/kg per Day   |                             |                         |                       |
| Placebo 12      | −1.3 (4.9) | 20  −1.0 (3.8) | 0.01 6 −0.7 (5.4) | 8  −0.7 (4.6) |
| 0.03 8          | −1.4 (4.1) | 8  −1.4 (4.1) | 0.10 13 −2.4 (5.5) | 16  −2.1 (5.0) |
| 0.30 8          | −7.1 (8.5) | 18  −3.3 (6.7) |

*LOCF indicates last observation carried forward; rL, recombinant methionyl human leptin.

**Figure 4. Relationships Between Recombinant Methionyl Human Leptin (rL) Dose and Body Composition (Fat Mass)**

In study part A among the lean and obese subjects, $P = .002$ for the change in fat mass and $P = .11$ for fat-free mass. In study part B, $P = .004$ for the change in fat mass and $P = .8$ for fat-free mass. Fat mass was measured by dual-energy x-ray absorptiometry. Gray line indicates baseline.
was reported by subjects treated at the highest doses of rL, suggesting that the weight loss effect may be due to a reduction in food consumption. However, the instrument used (48-hour dietary recall) is relatively insensitive, and there was considerable variability in the reduction of energy intake.

Considered a characteristic of the injection technique, injection site ecchymosis was the most common adverse effect and occurred among 71% of those treated with placebo and 62% of those treated with rL. Symptoms considered characteristic of subcutaneous administration of a protein, such as injection site erythema, pruritus, and inflammation, occurred with greater incidence in rL-treated subjects than in placebo-treated subjects. Injection site reactions did not appear to unblind the study as they were not unique to the subjects receiving rL. Injection site reactions were generally treated with topical creams and antihistamines, most resolved over a few weeks, and they did not appear to contribute significantly to the dropout rates.

Antibodies to leptin were observed in 38% and 71% of rL-treated subjects at 4 and 24 weeks, respectively; however, these antibody levels had no relationship with weight loss or overall adverse event incidence. At 24 weeks, antibody-positive subjects had a higher incidence of ISRs; however, the incidence of both ISRs and seroreactivity increased with dose, so a causal relationship of seroreactivity to dose should not be inferred. In subjects who tested positive for antibody formation, higher rL serum concentrations were observed on day 28 compared with day 1 and day 14 results. These data are consistent with pharmacokinetic data obtained in animals, which showed that following formation of antibodies against rL, serum concentrations of rL increased.

With the exception of 2 subjects who withdrew for ISRs and 1 who withdrew for palpitations, dropouts did not appear related to adverse events, and adverse events (other than ISRs) did not appear related to the rL dose. Subject withdrawals were greatest in the highest-dose cohort. The majority of withdrawals among obese subjects was between the initial 4-week part A and the 20-week part B study. We believe that injection volume or number of injections influenced the decision to withdraw. Sensitivity analyses using imputed values for subjects who withdrew led to similar conclusions about the dose-response relationship of rL treatment to weight loss.

Researchers have expressed some concern that leptin may exacerbate insulin resistance or contribute to type 2 diabetes. Based on OGTT performed at baseline and after 4 and 24 weeks of treatment with rL, we found no indication that exogenous leptin affected glycemic control. Because these subjects were selected based on expected normal glucose tolerance, it was not possible to document an improvement in abnormal glycemic control associated with treatment.

In conclusion, these results demonstrate that subcutaneous bolus injections of rL result in weight loss in some individuals, and show that the weight loss caused by rL may be due almost

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### Table 4. Subject Incidence of Injection Site Reactions (ISRs) for Obese Subjects

<table>
<thead>
<tr>
<th>Subject Incidence of ISRs*</th>
<th>rL Dosage, mg/kg per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n = 21)</td>
</tr>
<tr>
<td>Any ISR</td>
<td>16 (76)</td>
</tr>
<tr>
<td>Injection site</td>
<td></td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>15 (71)</td>
</tr>
<tr>
<td>Erythema</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Inflammation (induration)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Pain</td>
<td>4 (19)</td>
</tr>
<tr>
<td>Rash</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Reaction†</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Edema</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Subject incidence was defined as the number of subjects who experienced the indicated event at least once at any time during both parts of the study. rL indicates recombinant methionyl human leptin. All data are number (percentage).
†This term was used to capture other symptoms such as warm skin, dry skin, and flaky skin.

### Table 5. Maximum Serum Leptin Concentrations*

<table>
<thead>
<tr>
<th>Maximum Serum Leptin Concentration, ng/mL†</th>
<th>rL Dosage, mg/kg per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Subjects</td>
<td>Placebo</td>
</tr>
<tr>
<td>Baseline</td>
<td>37</td>
</tr>
<tr>
<td>Day 4</td>
<td>38</td>
</tr>
<tr>
<td>Week 4</td>
<td>35</td>
</tr>
<tr>
<td>Week 24‡</td>
<td>12</td>
</tr>
</tbody>
</table>

*All data are presented as mean (SD).
†Concentrations reported herein are the maximum value following the dose on the indicated days. Note that the assay did not distinguish between endogenous leptin and recombinant methionyl human leptin (rL).
‡Obese subjects only.
Entirely to fat loss. These results also suggest that rL has an acceptable short-term (≤6 months) safety profile. Although additional human studies of leptin analogs are necessary to determine its therapeutic potential for the treatment of obesity and diabetes, many questions remain about the possibility of using a leptin receptor agonist as a therapeutic agent to treat obesity. Our findings show, however, that some patients, across a wide range of body weights, respond to exogenous leptin administration.

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