Open-Label Pilot Study of the Safety and Efficacy of LDI-200 in the Treatment of Cancer-Associated Pain

Subcutaneous HCG plus levamisole (LDI 200) may stimulate the immune system to recognize and clear HCG, resulting in a positive tumor response.

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A 4-week open-label evaluation was conducted to determine the safety, tolerance, and efficacy of LDI-200 in adult patients with cancer-associated pain. All study subjects had pain not adequately controlled with conventional analgesics. After approval by an institutional review board and informed written consent by patients, a 7-day baseline evaluation was used to document patients' pain, emotional distress, and analgesic use. Patients were then administered 2 USP of human chorionic gonadotropin (HCG) as a 0.2-mL subcutaneous injection daily for 4 weeks and 50 mg levamisole hydrochloride once per week orally.

Seven patients with advanced malignancy participated in the study. Two patients had squamous cell carcinomas (lung and malar); one patient had astrocytoma; and four had adenocarcinomas (pancreatic, gastrointestinal, nasopharyngeal, and parotid). Patients were evaluated weekly for total opioid use and assessed with the Visual Analog Scale (VAS) and Karnofsky quality of life indicators, pre-injection, immediately after injection, and 1 hour after injection.

RESULTS

The two patients with squamous cell carcinoma showed neither a decrease in analgesic use nor improvements in pain or quality of life. The patient with astrocytoma remained on the protocol for 28 days until chemotherapy was required for tumor progression. Initial VAS 6 was reduced to 0 by the fourth week. This patient's analgesic requirement (acetaminophen 650 to 1300 mg/day) ceased, and the Karnofsky score increased from 80 to 90.

The patient with nasopharyngeal malignancy was dropped from the protocol on day 12 because of massive nasopharyngeal bleeding. There were no recorded improvements at the time of withdrawal. The remaining three patients showed decreased analgesic use (Table 1). VAS scores and Karnofsky quality of life indicators were dramatically

TABLE 1 Change in analgesic in oral morphine equivalents before and after LDI-200.

	Patient 1	Patient 2	Patient 3
Before LDI	360 MS Equiv.	310 MS Equiv.	2223 MS Equiv.
After LDI	120 MS Equiv.	270 MS Equiv.	1512 MS Equiv.

Patient 1 = pancreatic cancer; Patient 2 = GI cancer; Patient 3 = parotid cancer

TABLE 2 Visual Analog Scale and Numeric Pain Distress Scale.

	Patient 1	Patient 2	Patient 3
Day 1	2.3 / 4	1.2 / 1	7 / 4
Week 4	2.5 / 3	2.2 / 1	4 / 4
Week 9	–	1 / 0	0 / 0
Week 14	–	1 / 1	

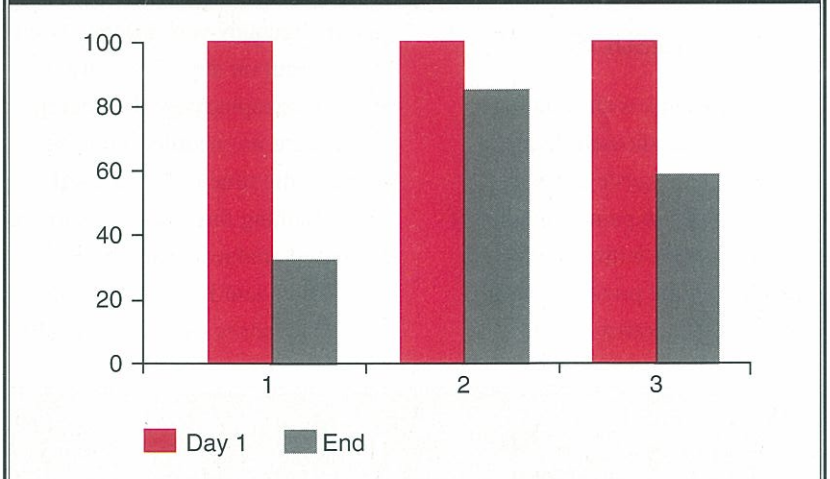
Patient 1 = pancreatic cancer; Patient 2 = GI cancer; Patient 3 = parotid cancer

TABLE 3 Karnofsky index changes.

	Patient 1	Patient 2	Patient 3
Day 1	60	70	50
Week 4	50	70	40
Week 9	–	80	–
Week 14	–	90	–

Patient 1 = pancreatic cancer; Patient 2 = GI cancer; Patient 3 = parotid cancer
Increases in Karnofsky index indicate improvements.

FIGURE 1 Percent change in analgesic use in oral morphine equivalents.



Patient 1 = pancreatic cancer; Patient 2 = GI cancer; Patient 3 = parotid cancer

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improved in patients with gastrointestinal and parotid adenocarcinomas, but not in the patient with the pancreatic adenocarcinoma (Tables 2 and 3).

DISCUSSION

It appears that LDI-200 is ineffective for either quality of life indicators, reductions in analgesic use (Figure 1), or decreases in pain for patients with squamous cell carcinoma; however, promise is likely in adenocarcinoma, since three study patients, despite tumor progression, showed measures of improvement. Two of the patients (gastrointestinal and parotid carcinoma) had improvements with all scales used for assessment. An effect on various endstage adenocarcinoma tumors despite different presentations implies a possible common denominator to nociception in some forms of cancerous pain. The mechanism of action of HCG is not known. Several investigators have implicated HCG as an immunosuppressant that allows malignant transformation. Small doses of subcutaneous HCG in the presence of levamisole may stimulate the immune system to recognize and clear HCG thus having an effect on responsive tumors. Perhaps with analgesia, changes occur in tumor cellular dynamics and secretion of nociceptive peptides.