RESULTS

Patient Demographics

This demographic column reflects data collected through April 15, 2009. To date, total device exposure is 33,491 days (approx. 163 patient years). Baseline demographics of the patient population are provided in Table 2 and were similar to other published studies involving implantable drug delivery systems (ECDs)1. The ratio of men to females is 1:1 in relation to the type and frequency of interatcive back pain and its underlying distribution in the general population.

Device Description

The Prometra Programmable Pump, developed by InMed Technologies Incorporated (MI: Oliver, NZ) is a pressure-driven, calibrated, microdispensing pump. This type of design is expected to provide a number of improvements over generations of programmable pumps, including:

- Non-compliant dosing chamber that provides meticulous measurement (no dilution)
- Fixed, controlled drug flow with electronic data output
- A reservoir that acts as a volume-control regulator in micro increments
- An isolated valve system robust to temperature and pressure changes
- Ability to completely shut down (save flow)

In addition to improved accuracy, it is expected to have microfluidic delivery capability, a long drug delivery life (10-15 years), and energy efficiency, relative light weight, and the ability to deliver advanced compounds, such as large-proteins.

METHODS

Protocol Design

The PUMP study is a prospective, multi-center, open-label evaluation of the Prometra Programmable Pump System in the administration of intrathecal morphine sulfate for the treatment of chronic intractable pain.

Seven centers participated in the study which began enrollment in March 2007 and finished in December 2007 (Table 1). One hundred and ten (110) patients met inclusion criteria and were enrolled with the Prometra Pump.

Upon implantation (Day 0), the pump was filled with an appropriate concentration of morphine sulfate and programmed for constant flow. Daily dosing was based on patient need and could be adjusted at any time throughout the course of the study. Patients attended follow-up visits at Day 10 (+5 days) to assess wound healing, and then monthly (+/−1 day) up to 6 months post-implantation to assess device performance, and refill the reservoir. During refill visits, the volume of residual drug in the pump was measured using the volume with syringe supplied with the device, and the delivered volume was calculated. After 6 months, patients entered the long-term phase of the study with visits scheduled every 3 months (+2 days). Data is managed and analyzed by an independent third-party clinical trials Functional (The Woodlands, TX).

Endpoints and Analysis

The primary endpoint of this accuracy-of-medication delivery was this measurement by comparing the volume of medicine programmed for delivery with the amount actually delivered. Pump refills were required monthly for the first six months post-implantation and then quarterly, until the device reaches market approval. Additional refills were allowed as needed to avoid interruption of therapy. Accuracy was measured using 1,000 refill visits from 107 patients.

The secondary endpoint addressed the efficiency of treatment, as measured by changes from baseline in three pain and quality of life assessments, the NRS, VAS, and ODI.

Table 2: Demographic (N=110)

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<th>Patient Number</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>CUP Score</th>
<th>ODI Score</th>
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</table>

For each patient, the pump was refilled with the appropriate concentration of morphine sulfate and programmed for a constant flow. The median programmed morphine dose is presented in Figure 1. The increase in median programmed morphine dose is significant (p<0.05).

Figure 1: Mean Dose Day 0 to Visit

To examine accuracy as a function of daily flow rate, programmed flow rates were divided into four groups with comparable numbers of visits (Figure 4). No significant differences were seen between flow rate groups (p>0.05).

Figure 3: Mean Accuracy vs. Flow Rate

Finally, accuracy was consistent as a function of residual volume (Figure 4). No significant differences were seen between residual volume categories (p>0.05). Notably, accuracy was consistently high in the highest residual volume category (p=0.015).

DISCUSSION

At the start of the current study, the Prometra Pump System has been shown to provide consistently accurate drug delivery, with mean accuracy of 97.4%, with a 90% confidence interval of 96.8–98.0%. Compared to current market-approved pumps, this is significantly higher. Accuracy is consistent over the 25-month period of the study, and was not significantly affected by flow rate or residual drug volume. The consistently accurate drug delivery at residual volumes under 2 mL. (Possible the potential for improved outcomes over currently marketed pumps, which recommend refills before the reservoir reaches such low volumes.1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14

Highly accurate dosing intuitively offers clinical benefits for patients with greater sensitivity to side effects or for patients at risk for non-compliance. Higher accuracy will improve outcomes when using drugs with higher potency or more narrow therapeutic windows, and may facilitate the clinical use and optimization of drug administration for particular pain conditions or patient subpopulations. It is unclear whether increased drug accuracy might also reduce the risk of granuloma formation, a phenomenon that is poorly understood but may be linked to drug concentration and exposure.

In addition to the accuracy and efficacy data, the Prometra System provided safe therapy for this patient population. No unexpected adverse events or deaths were attributed to the device or the procedure, and no pump failures were reported during the study. There have been no reports of major biological or symptomatic granuloma formation in this pivotal clinical study, which has recently surpassed 201 patient years of investigational experience. The adverse events and device-related complications reported were consistent with complications described in other studies involving ECDs.1, 2, 3

CONCLUSION

This study was sponsored and funded by InMed Technologies. CATHEDRAL Investigational Device, United for (or United States) Law to Investigational Use.