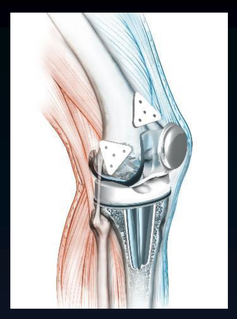

ATX101 Provided Sustained Pain Relief in TKA Patients: Results of an Exploratory Multicenter Double-Blind RCT

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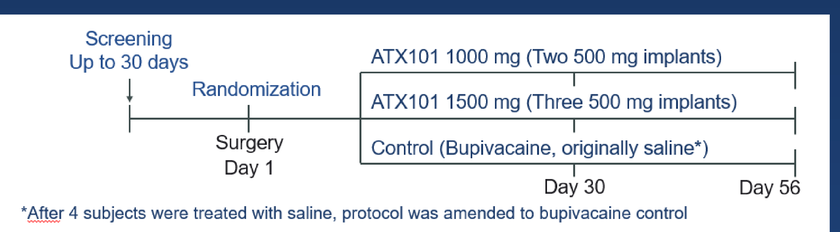
INTRODUCTION

- TKA is associated with pain that lasts weeks impacting rehabilitation and requires opioids with troubling AEs
- Current bupivacaine formulations last <4 days
- ATX101, a novel bupivacaine formulation, provides controlled release of bupivacaine locally for approximately 4 weeks post-surgery
- Safety, PK, efficacy, opioid consumption and function were evaluated in a double-blind randomized controlled trial (NCT05260008)
- ATX101 is an investigational product that has not been approved by US FDA, or in any other country

OBJECTIVES

- Exploratory study to compare PK, safety, and efficacy of ATX101 (1000 mg & 1500 mg) to bupivacaine HCl (bupivacaine) or placebo in subjects undergoing unilateral TKA
- To compare opioid consumption across cohorts
- To estimate the sample size, determine dose and primary endpoint duration for an adequate well-controlled registration trial

METHODS



Monitoring: Full safety, PK & cardiac monitoring in PACU to 96 h
Clinic/home health Days 6, 8, 15, 22, 30 & 56

Multimodal Analgesic Regimen

- Preoperative
  - Acetaminophen 1000 mg & celecoxib 200 mg
  - Bupivacaine spinal anesthesia, no opioids
  - Spinal anesthesia with general anesthesia optional
- Intraoperative
  - No opioids
  - ATX101 implant or control via local infiltration and/or adductor canal block, per randomization
- Postoperative
  - Celecoxib 200 mg bid for 30 days
  - Acetaminophen 500 mg/4 hour or 1,000 mg/6-8 hours, not to exceed 3000 mg/24 hours for 30 days
- Rescue (stepwise, as needed)
  - Oxycodone IR 5-10 mg every 4-6 hours as needed
  - Oral hydromorphone (2 or 4 mg) every 4-6 hours as needed
  - In-hospital IV opioids allowed per standard of care

Efficacy Analysis

- Area under the curve for NRS-R through Day 30 censored for opioid use
- Opioid consumption & functional assessments through Day 56
- ATX101 arms and control arms combined to increase power of exploratory trial design

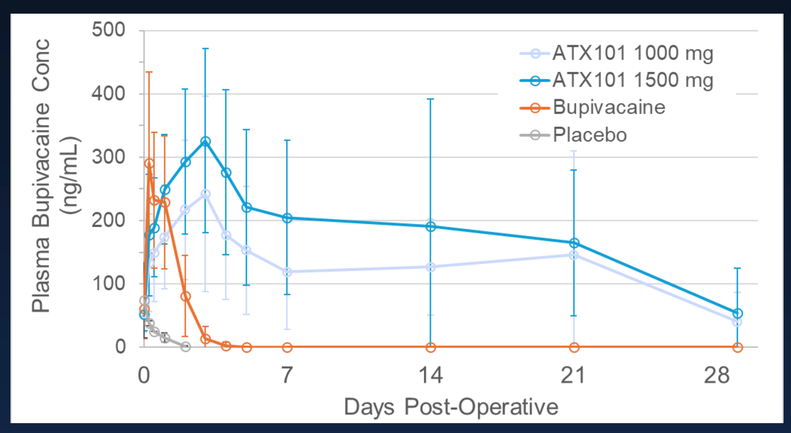


Fig 1. Plasma bupivacaine levels (mean ± SD) through Day 30

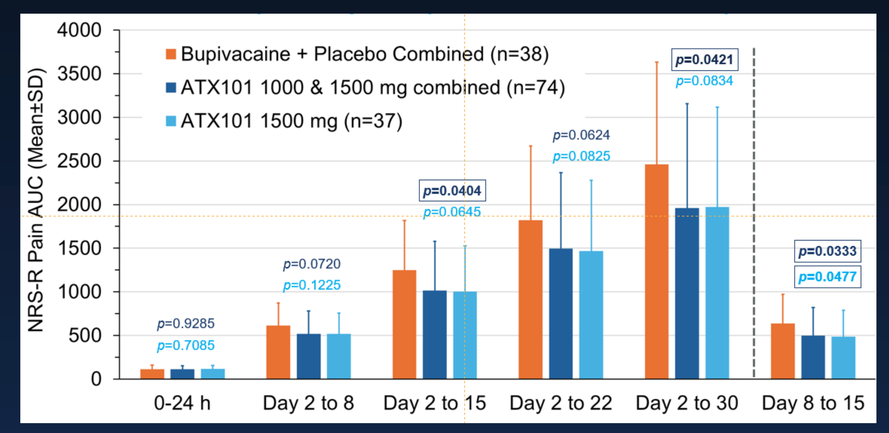
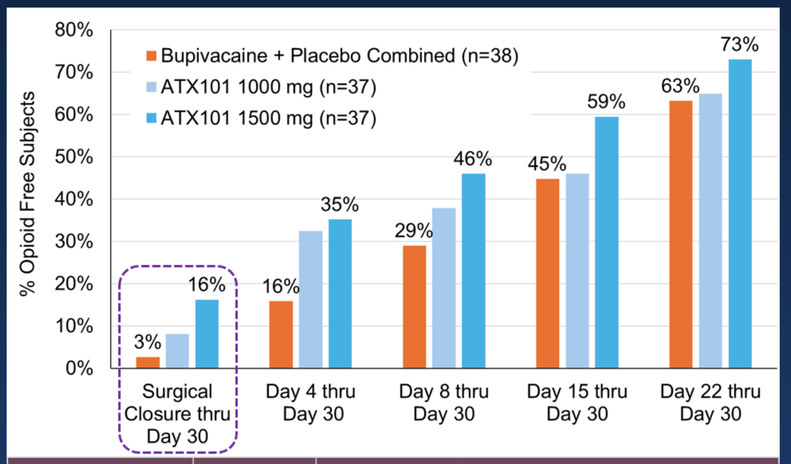


Fig 2. NRS-R AUC censored for opioids (mean ± SD)



Study Arm	Overall AEs	Opioid-related AEs		
		Total	Constipation	Vomiting
ATX101 1500 mg	68%	38%	10%	0%
Bupivacaine	82%	47%	30%	12%

Fig 3. % of subjects opioid free from various time points thru Day 30 and % of subjects with opioid-related adverse events

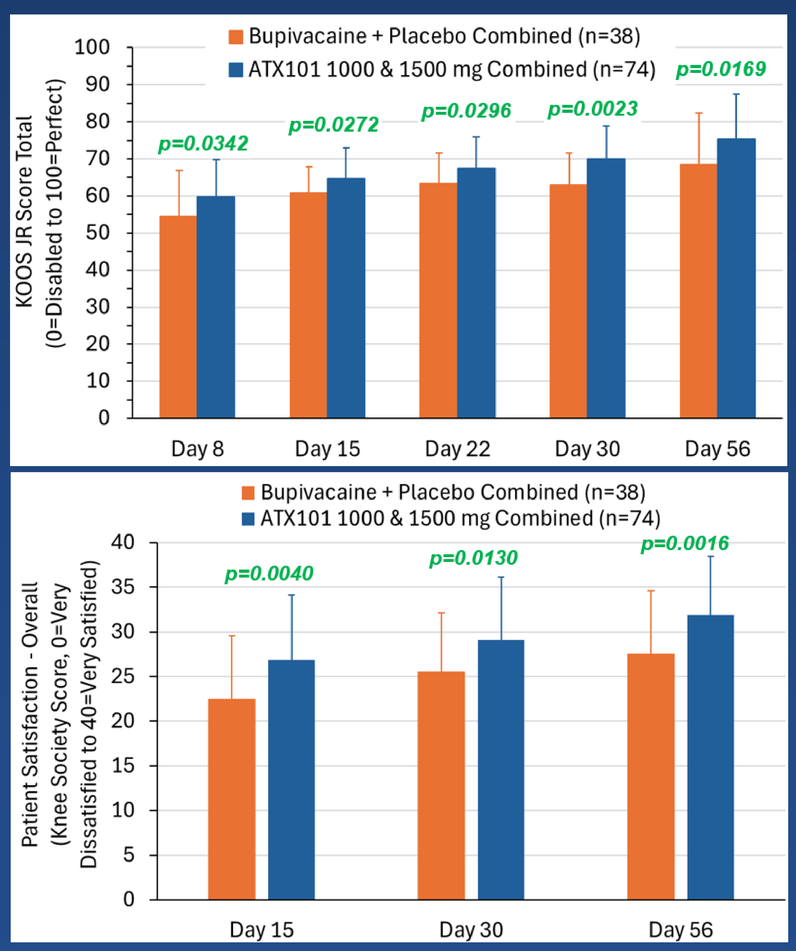


Fig 4. Better functional outcomes for ATX101 (1000 mg & 1500 mg groups combined) vs combined control as assessed by Total KOOS JR Score and Overall Patient Satisfaction (KSS) (mean ± SD)

RESULTS

- Demographics (n=112): 56% female; average age = 67.8 years; average BMI = 31.4
- Adverse events (AEs):
  - Fewer subjects in 1500 mg group (67.6%) had AEs versus 1000 mg (82.4%) or control groups (bupivacaine = 82.4%; placebo = 100%)
  - Most common (>5 subjects): nausea, constipation, procedural pain, contusion, dizziness, joint swelling, arthralgia, vomiting, diarrhea, implant site swelling, pain in extremity, fatigue, muscle spasm, peripheral swelling
  - No treatment related SAEs
- Plasma PK showed sustained, controlled release of bupivacaine from ATX101 and C_{max} was below levels for Local Anesthetic Systemic Toxicity (Fig 1)
- Pain AUC NRS-R for ATX101 was lower from 24 hours through Day 30 (Fig 2)
- In the 1500 mg group, 16% of subjects were opioid free from surgical closure to Day 30 (dashed box Fig 3) and, compared to control, more subjects discontinued opioids sooner and had fewer opioid-related AEs (Fig 3 table)
- 70% of subjects in 1500 mg group reached 90° flexion two weeks earlier than the control group (data not shown)
- Nominal statistical significance between ATX101 (combined doses) and control was demonstrated on KOOS JR as early as 8 days (Fig 4, upper) and multiple subscales of the KSS, including Satisfaction (Fig 4, lower)
- In a survey conducted after study completion, surgeons were satisfied or very satisfied with ease and time (~5 min/1500 mg) to place ATX101

CONCLUSIONS

- ATX101 appeared to be generally safe & well tolerated
- ATX101 PK showed levels of bupivacaine out to 3 weeks that are consistent with levels associated with the acute analgesic effect of bupivacaine
- ATX101 1500 mg demonstrated a strong clinically meaningful signal for efficacy by NRS-R AUC for pain intensity, reduced opioid consumption, fewer AEs, decreased opioid related AEs, and improved functional outcomes
- Safety and efficacy of ATX101 1500 mg will be evaluated in an upcoming Phase 2b registration clinical trial

Allay Therapeutics funded & conducted this clinical trial