A 5-year-old girl weighing 18.3 kg with relapsed abdominal neuroblastoma was referred to the Pain Service for recently exacerbated abdominal pain due to a large abdominal mass. Fentanyl PCA was started 5 mcg q 15 minutes. On day 5 a continuous infusion 10 mcg/hr was started and boluses were 15 mcg q 15 minutes (average 19.3 mcg/hr). Over the subsequent 21 days increments of the basal rate and the bolus size were made to ensure about 2/3 of the needs as infusion and 1/3 as boluses while maintaining low pain scores. The hourly total average dose (infusion and boluses) escalated from 19.3 mcg/hr on day 5 to 65 mcg/hr on day 11, 110 mcg/hr on day 14, 150 mcg/hr on day 18, 168 mcg/hr on day 19, 260 mcg/hr on day 20, 650 mcg/hr on day 22, 1000 mcg/hr on day 25, and 1800 mcg/hr on day 26. On day 26 infusion rate was adjusted from 600 to 3000 mcg/hr, with boluses of 250 mcg q 5 minutes. Since anxiety contributed to the severity of pain, lorazepam 0.5 mg IV bid was started on day 7 and was changed to an infusion 0.5 mg/hr on day 26. Due to the large volume of fentanyl infusion (3000 mcg/hr or 60 ml/hr) the opioid was changed to sufentanyl. Based on an equianalgesic ratio of 1 to 10, this strategy permitted lower infusion rates. Due to the rapidly escalating pain, the sufentanyl infusion was increased from 500 mcg/hr with 40 mcg boosts q 5 minutes (average of 514 mcg/hr) on day 27 to 650 mcg/hr with 100 mcg boluses q 5 minutes (average of 733 mcg/hr) on day 32. The midazolam infusion was increased from 0.5 to 1 mg/hr on day 32.

Due to the opioid escalation, in order to partially reverse opioid tolerance, a low dose ketamine infusion was started on day 32 at 2 mg/hr or 0.11 mg/kg/hr, for sub hypnotic, sub anesthetic effects. Within the first few hours of ketamine infusion the sufentanyl infusion was decreased from 650 mcg/hr to 450 mcg/hr with stable pain scores. The overall decrease in the sufentanyl use was from 733 mcg/hr to 450 mcg/hr or a decrease of opioid use by 39% in the first 24 hours of ketamine use. On the second day of ketamine infusion the sufentanyl use was 404 mcg/hr or a decrease of 45%. The ketamine infusion of 2 mg/hr was administered for 7 days with a brief increase to 2.5 mg/hr (0.13 mg/kg/hr) during the last hours of life. The midazolam infusion was continued at 1 mg/hr until day 36, and 1.5 mg/hr from day 36 to 38. Due to a shortage of sufentanyl on day 34 the sufentanyl infusion of 400 mcg/hr was replaced with sufentanyl 150 mcg/hr and fentanyl infusion 1500 mcg/hr while the ketamine and midazolam infusions were continued. An overall opioid dose reduction of 25% was anticipated based on the opioid rotation advantage, and therefore we calculated 150 mcg/hr sufentanyl and 1500 mcg/hr fentanyl to be equivalent to 400 mcg/hr sufentanyl rather than 300 mcg/hr sufentanyl. The sufentanyl PCA still had the bolus option for exacerbations of pain. During the last 7 days of life, the pain scores were consistently low, while maintaining an acceptable level of sedation and interaction with the family members.

Summary: We present a case of severe abdominal pain in a 5-year-old girl with neuroblastoma in which the addition of ketamine infusion decreased opioid use by 45%. Ketamine has opioid-tolerance reversal effects based on the NMDA receptor antagonist action.