**Supplemental Material**

**Perioperative pain protocol for patients undergoing an open partial hepatectomy for living donation at our institution.**

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| **Perioperative Pain Protocol for open partial hepatectomy for living donation** |
| Preoperative |
|  | Acetaminophen 1000mg PO |
|  | Pregabalin 75mg PO |
|  | Celecoxib 200mg PO (If not prior kidney donor) |
| Intra-operative |
|  | Fentanyl 50-100mcg at induction |
|  | Ketamine 0.25mg/kg bolus followed by infusion of 0.1mg/kg/h\* |
|  | Lidocaine 1mg/kg bolus followed by infusion of 1mg/kg/h\* |
|  | Dexmedetomidine infusion 0.2-0.5 mg/kg/h\* |
|  | Bupivacaine at surgical site per surgical team |
| Post-operative |
|  | Hydromorphone PCA per surgical team |
|  | Ketorolac 15mg IV q6h |

\*Infusions stopped when hepatic graft leaves the field

**LC-MS/MS Analysis of Lidocaine and Lidocaine metabolites (MEGX and GX)**

Lidocaine and its metabolites glycinexylidide (GX) and monoethylglycinexylidide (MEGX) were quantified using high-performance liquid chromatograph- tandem mass spectrometry LC-MS/MS by iC42 Clinical Research and Development (Aurora, CO, USA). The assay in brief:

Reference compounds for lidocaine were purchased from Sigma Aldrich (St. Louis, MO, USA) and for GX and MEGX as well as for the corresponding internal standards lidocaine-d6 and monoethylglycinexylidide-d5 (MEGX-d5) from Toronto Research Chemicals (Toronto, ON, Canada).

To 200 µL of each EDTA plasma study, calibrator, quality control, blank and zero sample, 600 µL of a methanol protein precipitation solution containing the internal standards (100 ng/mL lidocaine-d6 and 250 ng/mL MEGX-d5) were added. Samples were then vortexed for 5 min, centrifuged at 16,000 g at 4°C for 10 min. Hereafter, the supernatants were transferred into 2-mL glass HPLC injection vials. The extracted samples were analyzed using an LC-MS/MS system composed of a PAL StkCooler autosampler (CTC Analytics LEAP Technologies, Carrboro, NC, set to 4°C) with integrated 6-port VICI switching valve (Valco Instruments, Houston, TX) and an Agilent series 1100 HPLC system (Agilent Technologies, Santa Clara, CA) connected via a turbo flow electrospray ionization source to a Sciex API 5000 triple stage quadrupole mass spectrometer (Sciex, Concord, ON, Canada). The connections of the switching valve are shown in the Figure below.

*Connections and positions of the column switching valve.*

On the left, the loading position and online extraction is shown, on the right, after the switch, the analytes are backflushed from the online extraction column and separated on the analytical column.



For online solid phase extraction, 100 µL of the extracted samples were injected and washed onto an extraction column (Zorbax XDB C8, 4.6 · 50 mm) with a mobile phase of 10% methanol containing 0.1% formic acid (mobile phase B) and 90% of 0.1% formic acid in HPLC grade water (mobile phase A). The flow was 3 mL/min and the temperature for the extraction column was set to room temperature. After 1 min, the switching valve was activated and the analytes were eluted in the backflush mode from the extraction column onto the 4.6 · 150 mm analytical column filled with C8 material of 5 μm particle size (Zorbax XDB C8, Agilent Technologies, Palo Alto, CA).

The gradient elution started from 40% of mobile phase B and increased to 55% within 3.7 min and 90% within 0.3 min. The column was re-equilibrated to 40% after 0.5 min. The flow rate was 1.0 mL/min and the analytical column was kept at 40°C. For detection, the following ion transitions were monitored in the positive multiple reaction monitoring (MRM) mode: m/z= 235.2 [M+H]+ 🡪86.1 (lidocaine), m/z= 207.2 [M+H]+ 🡪58.0 (MEGX), m/z= 179.1 [M+H]+ 🡪122.0 (GX), m/z= 241.2 [M+H]+ 🡪86.1 (lidocaine-d6) and m/z= 212.2 [M+H]+ 🡪63.0 (MEGX-d5). Declustering potentials and collision energies were set to 80V and 25V for lidocaine and lidocaine-d6, 51V and 27V for MEGX and MEGX-d5, 41V and 19V for GX.

Lidocaine and lidocaine metabolites concentrations were quantified using the two calibration curves included in each analytical run and that were constructed by plotting nominal concentration *versus* the analyte/ internal standard peak area ratios (response) using a quadratic fit and 1/x weight. All calculations were carried out using the AB Sciex Analyst Software (version 1.6.2). The range of reliable quantification was (lower limit of quantification- upper limit of quantification): 25 – 10,000 ng/mL for Lidocaine, MEGX and GX. There were no significant carry-over, matrix effects or matrix interferences. The extracted samples were stable in the autosampler at 4°C for at least 48 hours.

All sample runs met the following acceptance criteria:

* The assay was under control and all corrective actions, if applicable, had successfully been resolved.
* Acceptable system/ instrument suitability test
* Linearity of the calibration curve was better than r= 0.99.
* Low calibration sample signal to noise ratio of at least 8:1.

No significant interference in blank or zero samples (less than 20% of the signal at the lower limit of quantification and the response at the retention time of the internal standard in the blank did not exceed 5% of the average internal standard responses in the calibrators and quality control samples).

* No significant carry-over (less than 20% of the signal at the lower limit of quantification)
* Accuracy of 3/4 of calibration samples (=75%) was better than ±15% from nominal, except for the LLOQ sample, which was better than ±20%.
* 2/3 quality control samples in an analytical batch were within 15% of the nominal concentration
* ≥ 50% of QCs per level were within ± 15% of their nominal concentrations.