Laparoscopic nephrectomy

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CASE PRESENTATION
A 66-year-old female with a BMI of 34 presented with vague abdominal pain and a single episode of gross hematuria. Past medical history included peptic ulcer disease, coronary artery disease, obesity and hypertension. Her physical exam was unremarkable.

Abdominal CT scan revealed an 8.5 cm solid right renal mass with no evidence of metastatic disease on staging evaluation. Inferior vena cava and right renal vein were clear of tumor thrombus.

DIAGNOSIS AND RECOMMENDED PROCEDURE
• Confirmed renal cell carcinoma with no evidence of metastatic disease (Stage T2a)
• Right laparoscopic radical nephrectomy

PATIENT’S PERIOPERATIVE ANALGESIC PROTOCOL

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>PreOp</th>
<th>IntraOp</th>
<th>PostOp Day 1†</th>
<th>PostOp Day 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>OFIRMEV® (acetaminophen) injection</td>
<td>1 g</td>
<td>1 g q6h</td>
<td>1 g q6h</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(prior to closure)</td>
<td>for 24 h</td>
<td>for 24 h</td>
<td></td>
</tr>
<tr>
<td>IV fentanyl</td>
<td>100 μg (induction)</td>
<td>150 μg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local anesthesia</td>
<td>Bupivacaine 0.25% 30 mL total (given at closure)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV morphine PCA</td>
<td>38 mg</td>
<td></td>
<td>14 mg</td>
<td></td>
</tr>
<tr>
<td>IV ketorolac</td>
<td>15 mg q6h</td>
<td>for 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PO oxycodone</td>
<td>10 mg q3h prn</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† PostOp Day 1 defined as 0-24h after surgery.

• Do not exceed the recommended maximum daily limits of acetaminophen by all routes. The maximum total daily dose of OFIRMEV for adults ≥50kg is 4000 mg.

INDICATIONS AND USAGE
OFIRMEV® (acetaminophen) injection is indicated for the management of mild to moderate pain, management of moderate to severe pain with adjunctive opioid analgesics, and reduction of fever.

IMPORTANT RISK INFORMATION

WARNING: RISK OF MEDICATION ERRORS AND HEPATOTOXICITY
Take care when prescribing, preparing, and administering OFIRMEV Injection to avoid dosing errors which could result in accidental overdose and death. In particular, be careful to ensure that:
• the dose in milligrams (mg) and milliliters (mL) is not confused;
• the dosing is based on weight for patients under 50 kg;
• infusion pumps are properly programmed; and
• the total daily dose of acetaminophen from all sources does not exceed maximum daily limits.

OFIRMEV contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed the recommended maximum daily limits, and often involve more than one acetaminophen-containing product.

Please see additional Important Risk Information on reverse and in accompanying Full Prescribing Information.

* This case study is intended only to provide healthcare professionals with an example of the use of OFIRMEV (acetaminophen) injection in the treatment of one specific patient. The outcomes described may not be representative of, and may differ significantly from, outcomes that may be obtained in treating other patients. This case study is not intended to provide specific treatment advice, recommendations, or opinions, and should not replace a clinician’s judgment with respect to the treatment of any particular patient.
### PostOp Outcomes

<table>
<thead>
<tr>
<th>PAIN ASSESSMENT*</th>
<th>OPIOID CONSUMPTION</th>
<th>PATIENT SATISFACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>• PostOp Day 0: 3/10 in PACU; decreased to 2/10 at PostOp Hour 12</td>
<td>• PostOp Day 1: 38 mg IV morphine via PCA</td>
<td>• “Excellent” rating for pain control on a 4-point categorical scale</td>
</tr>
<tr>
<td>• PostOp Day 1: 5/10 on first ambulation; decreased to 2/10 pain at rest</td>
<td>• PostOp Day 2: 14 mg IV morphine via PCA, 10 mg PO oxycodone</td>
<td></td>
</tr>
<tr>
<td>• PostOp Day 2: 3/10 on ambulation; decreased to 2/10 pain at rest</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on a 10-point visual analog scale (VAS).

### PATIENT AMBULATION/DISCHARGE

- Patient was discharged from the PACU after 45 minutes. The patient was able to ambulate with assistance on PostOp Day 1 and without assistance on PostOp Day 2. Total length of hospital stay was 2 days.

### IMPORTANT RISK INFORMATION

#### CONTRAINDICATIONS

- Acetaminophen is contraindicated in patients with:
  - known hypersensitivity to acetaminophen or to any of the excipients in the intravenous (IV) formulation.
  - severe hepatic impairment or severe active liver disease.

#### WARNINGS AND PRECAUTIONS

- Administration of acetaminophen in doses higher than recommended may result in hepatic injury, including the risk of liver failure and death. Do not exceed the maximum recommended daily dose of acetaminophen. The maximum recommended daily dose of acetaminophen includes all routes of acetaminophen administration and all acetaminophen-containing products administered, including combination products. Dosing errors could result in accidental overdose and death.
- Use caution when administering acetaminophen in patients with the following conditions: hepatic impairment or active hepatic disease, alcoholism, chronic malnutrition, severe hypovolemia (e.g., due to dehydration or blood loss), or severe renal impairment (creatinine clearance ≤ 30 mL/min).
- Rarely, acetaminophen may cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Hypersensitivity and anaphylaxis associated with the use of acetaminophen have been reported. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, and pruritus. The antipyretic effects of OFIRMEV may mask fever.
- **Serious adverse reactions** may include hepatic injury, serious skin reactions, hypersensitivity, and anaphylaxis. **Common adverse reactions** in adults include nausea, vomiting, headache, and insomnia. **Common adverse reactions** in pediatric patients include nausea, vomiting, constipation, pruritus, agitation, and atelectasis.

### USE IN SPECIFIC POPULATIONS

- Pregnancy: Pregnancy Category C. OFIRMEV should be given to a pregnant woman only if clearly needed.
- Breast Feeding: While studies with OFIRMEV have not been conducted, acetaminophen is secreted in human milk in small quantities after oral administration.
- Pediatrics: The effectiveness of OFIRMEV for the treatment of acute pain and fever has not been studied in pediatric patients < 2 years of age.

Please see additional Important Risk Information, including boxed warning, on reverse side and in accompanying Full Prescribing Information.
5.2 Serious Skin Reactions

CONTRAINDICATIONS

OFIRMEV (acetaminophen) Injection should be administered only as a 15-minute intravenous infusion. Do not add other medications to the OFIRMEV solution. Use aseptic technique when administering (see Dosage and Administration (2)).

The following additional treatment-emergent adverse reactions were reported by pediatric subjects treated with OFIRMEV: 1° Stevens-Johnson Syndrome (SJS), 2° toxic epidermal necrolysis (TEN), 3° erythema multiforme, 4° acute generalized exanthematous pustulosis (AGEP), 5° drug reaction with eosinophilia and systemic symptoms (DRESS). Patients should be informed about the signs of Stevens-Johnson syndrome, and use of the drug should be discontinued at the first appearance of rash or any other sign of hypersensitivity.

5.2 Serious Skin Reactions

Rash, acneiform eruptions may occur. Frequent and generalized pruritus and Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in post-marketing settings in patients treated with acetaminophen-containing products. Acneiform eruptions and rash (including erythema multiforme and toxic epidermal necrolysis) may occur with doses of acetaminophen above 4 g daily. Doses of 4 g acetaminophen daily or more in adults have been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of these cases have been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of these cases have been associated with cases of acute liver failure, at times resulting in liver transplant and death.

6.1 Clinical Trial Experience

When used concomitantly with other medications or products containing acetaminophen, the total daily dose of acetaminophen from all products should not exceed the maximum daily dose recommended in this labeling. The total daily dose of acetaminophen from all products should not exceed the maximum daily dose recommended in this labeling.

6.1 Clinical Trial Experience

Use caution when administering acetaminophen in patients with the following conditions: hepatic impairment or active hepatic disease (except for acute alcoholic hepatitis), alcoholic cirrhosis or other causes of severe hepatic injury, hypothyroidism (e.g., due to dehydration or blood loss), or severe renal impairment (creatinine clearance ≤ 30 mL/min). See "Use in Specific Populations: Renal Impairment" and "Use in Specific Populations: Hepatic Impairment".

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OFIRMEV during labor and delivery; therefore, it should be used in such settings only after a careful benefit-risk assessment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnant rats received oral acetaminophen throughout gestation at doses of 1.2-times the MHDD (based on a body surface area comparison), areas of necrosis occurred in both the liver and kidney of pregnant rats and fetuses. These effects did not occur in animals that received oral acetaminophen at doses 0.3-times the MHDD, based on a body surface area comparison. A dose-related reduction in body weight was observed in pregnant mice that received oral acetaminophen at doses 0.3- and 1.0-times the MHDD, based on a body surface area comparison. In contrast, there was no statistical evidence of carcinogenic activity based on increased incidences of mononuclear cell leukemia at 24 times the maximum human daily dose (MHDD) of 450 mg/kg/day, based on a body surface area comparison. In contrast, there was no evidence of carcinogenic activity in male rats (10.7 times the MHDD, based on a body surface area comparison).

8.2 Labor and Delivery

There are no adequate and well-controlled studies with OFIRMEV during labor and delivery; therefore, it should not be used in such settings only after a careful benefit-risk assessment.

14 CLINICAL STUDIES

Pharmacokinetic parameters of OFIRMEV in a 50 mg/kg dose in hemophilic mice showed no clinically significant changes in bleeding time after retesting multiple doses of OFIRMEV. The maximum concentration (Cmax) occurs at the end of the 8 hour period of continuous infusion of OFIRMEV. Compared to the same dose of oral acetaminophen, the Cmax following oral administration is much lower than oral acetaminophen exposure (area under the concentration time curve [AUC] is lower).

PHARMACOKINETICS

The pharmacokinetics of OFIRMEV have been studied in adults and healthy subjects and patients with hemophilia showed no significant changes in bleeding time after retesting multiple doses of OFIRMEV. The maximum concentration (Cmax) occurs at the end of the 8 hour period of continuous infusion of OFIRMEV. Compared to the same dose of oral acetaminophen, the Cmax following oral administration is much lower than oral acetaminophen exposure (area under the concentration time curve [AUC] is lower).

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