## **FIGURE 1**. Study flow diagram.

PaCO<sub>2</sub>: partial pressure of arterial carbon dioxide; PaO<sub>2</sub>: partial pressure of arterial oxygen; PetCO<sub>2</sub>: partial pressure of end-tidal carbon dioxide; RD: respiratory depression; RR: respiratory rate; SaO<sub>2</sub>: arterial oxygen saturation.

**FIGURE 2**. Effect of opioid treatment in patients with advanced disease on a) partial pressure of arterial carbon dioxide (PaCO<sub>2</sub>); b) partial pressure of end-tidal carbon dioxide (PetCO<sub>2</sub>). E: measured on exertion; R: measured at rest.

**FIGURE 3**. Effect of opioid treatment in patients with advanced disease on a) partial pressure of arterial oxygen (PaO<sub>2</sub>); b) arterial oxygen saturation (SaO<sub>2</sub>); c) respiratory rate (RR). E: measured on exertion; N: nebulized administration; R: measured at rest; S: systemic administration.