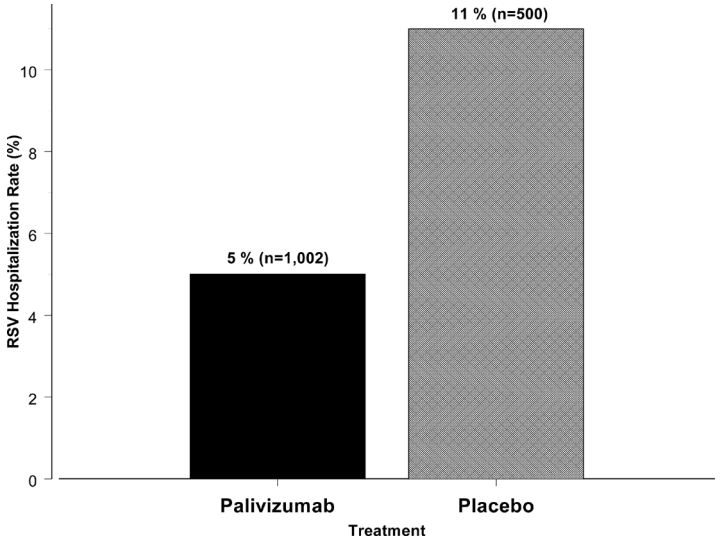

Figure 2 RSV hospitalization rates by palivizumab (15 mg/kg *IM*, monthly for 5 months) and placebo, $p < 0.0001$, 2-sided Fisher's exact test. (From Ref. 29.)

endpoint in human patients, the utilization of the preclinical information seemed reasonable.

Using 15 mg/kg as the human effective dose based on the preclinical database, a randomized, double-blind, placebo-controlled, multiple-dose (IM monthly injection for 5 months) phase III study of palivizumab was conducted in infants and children at high risk for severe RSV disease. The RSV hospitalization rate was used as the primary endpoint, and was statistically lower in the palivizumab treated group compared to that in the placebo-treated patients (Fig. 2), confirming that the dose selection approach was appropriate. This palivizumab case adequately exemplified how informative the preclinical database can be to select the human effective dose when the clinical dose–response studies are difficult or impossible to conduct.

2. UTILIZING THE PRECLINICAL DATABASE TO SUPPORT THE EFFICACY CLAIM FOR REGULATORY APPROVAL

Preclinical efficacy findings, if coupled with the well understood pathophysiology of a disease and the mechanism of action of a drug, could serve as the confirmatory evidence to support the conduct of a single phase III clinical trial for regulatory approval (30). This is a huge saving in terms of both time and resources for drug developers given that the current FDA position is to require at least two adequate and well-controlled phase III studies, each