

## Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial

Jörg D Leuppi, Philipp Schuetz, Roland Bingisser, Michael Bodmer, Matthias Briel, Tilman Drescher, Ursula Duerring, Christoph Henzen, Yolanda Leibbrandt, Sabrina Maier, David Miedinger, Beat Müller, Andreas Scherr, Christian Schindler, Rolf Stoeckli, Sebastien Viatte, Christophe Von Garnier, Michael Tamm & Jonas Rutishauser

### IMPORTANCE

International guidelines advocate a 7- to 14-day course of systemic glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease (COPD). However, the optimal dose and duration are unknown.

### OBJECTIVE

To investigate whether a short-term (5 days) systemic glucocorticoid treatment in patients with COPD exacerbation is noninferior to conventional (14 days) treatment in clinical outcome and whether it decreases the exposure to steroids. DESIGN, SETTING, AND PATIENTS REDUCE: (Reduction in the Use of Corticosteroids in Exacerbated COPD), a randomized, noninferiority multicenter trial in 5 Swiss teaching hospitals, enrolling 314 patients presenting to the emergency department with acute COPD exacerbation, past or present smokers ( $\geq 20$  pack-years) without a history of asthma, from March 2006 through February 2011.

### INTERVENTIONS

Treatment with 40 mg of prednisone daily for either 5 or 14 days in a placebo-controlled, double-blind fashion. The predefined noninferiority criterion was an absolute increase in exacerbations of at most 15%, translating to a critical hazard ratio of 1.515 for a reference event rate of 50%.

### MAIN OUTCOME AND MEASURE

Time to next exacerbation within 180 days.

### RESULTS

Of 314 randomized patients, 289 (92%) of whom were admitted to the hospital, 311 were included in the intention-to-treat analysis and 296 in the per-protocol analysis. Hazard ratios for the short-term vs conventional treatment group were 0.95 (90% CI, 0.70 to 1.29;  $P = .006$  for noninferiority)

in the intention-to-treat analysis and 0.93 (90% CI, 0.68 to 1.26;  $P = .005$  for noninferiority) in the per-protocol analysis, meeting our noninferiority criterion. In the short-term group, 56 patients (35.9%) reached the primary end point; 57 (36.8%) in the conventional group. Estimates of reexacerbation rates within 180 days were 37.2% (95% CI, 29.5% to 44.9%) in the short-term; 38.4% (95% CI, 30.6% to 46.3%) in the conventional, with a difference of -1.2% (95% CI, -12.2% to 9.8%) between the short-term and the conventional. Among patients with a reexacerbation, the median time to event was 43.5 days (interquartile range [IQR], 13 to 118) in the short-term and 29 days (IQR, 16 to 85) in the conventional. There was no difference between groups in time to death, the combined end point of exacerbation, death, or both and recovery of lung function. In the conventional group, mean cumulative prednisone dose was significantly higher (793 mg [95% CI, 710 to 876 mg] vs 379 mg [95% CI, 311 to 446 mg],  $P < .001$ ), but treatment-associated adverse reactions, including hyperglycemia and hypertension, did not occur more frequently.

#### CONCLUSIONS AND RELEVANCE

In patients presenting to the emergency department with acute exacerbations of COPD, 5-day treatment with systemic glucocorticoids was noninferior to 14-day treatment with regard to reexacerbation within 6 months of follow-up but significantly reduced glucocorticoid exposure. These findings support the use of a 5-day glucocorticoid treatment in acute exacerbations of COPD.

#### TRIAL REGISTRATION

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