exacerbation rate, but SFC users had a statistically significant reduction in all-cause mortality. Survival in the INSPIRE study was captured as a safety measure, so this observation has also not received much attention. Survival is a difficult and expensive outcome to capture as a primary outcome in a randomised clinical trial, and unfortunately we are not likely to see more survival studies in COPD any time soon.

Several retrospective studies have examined the survival benefit of specific treatments in COPD, with mixed results. Some have found a survival benefit with inhaled corticosteroids with or without long-acting β agonists, but others employing very different methods have not found a benefit.^{8,9} Although these studies provide insight into the 'real-life' impact of treatments in the general population, the biases inherent to retrospective study designs and controversies around appropriate analysis techniques leave much uncertain.

It is interesting to speculate on what specific interventions most improve the chances for improved survival in COPD. Is

it long-acting maintenance medications? Exercise rehabilitation? Improved attention to co-morbidities? Perhaps we will never prove that any single invention is sufficient by itself; maybe it takes multiple approaches implemented simultaneously. Whatever the case, success begins with belief by the doctor that treatment is effective, and confidence that we can make a difference for our patients with COPD.

Hope! Of all ills that men endure,
The only cheap and universal cure.

— Abraham Cowley

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REFERENCES

1. **Celli BR.** Update on the management of COPD. *Chest* 2008;**133**:1451–62.
2. **US Preventive Services Task Force.** Screening for chronic obstructive pulmonary disease using spirometry: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2008;**148**:529–34.
3. **Almagro P, Salvadó M, Garcia-Vidal C, et al.** Recent improvement in long-term survival after a COPD hospitalisation 2010;**65**:298–302.
4. **Global Initiative for Chronic Obstructive Lung Disease (GOLD).** Global Strategy for Diagnosis, Management and Prevention of COPD. Updated 2009. www.goldcopd.com (accessed 4 Dec 2009).
5. **Calverley PM, Anderson JA, Celli B, et al.** Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med* 2007;**356**:775–89.
6. **Celli B, Decramer M, Kesten S, et al; UPLIFT Study Investigators.** Mortality in the 4-year trial of tiotropium (UPLIFT) in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2009;**180**:948–55.
7. **Wedzicha JA, Calverley PM, Seemungal TA, et al; INSPIRE Investigators.** The prevention of chronic obstructive pulmonary disease exacerbations by salmeterol/fluticasone propionate or tiotropium bromide. *Am J Respir Crit Care Med* 2008;**177**:19–26.
8. **Sin DD, Wu L, Anderson JA, et al.** Inhaled corticosteroids and mortality in chronic obstructive pulmonary disease. *Thorax* 2005;**60**:992–7.
9. **Mapel DW, Nelson LS, Lydick E, et al.** Survival among COPD patients using fluticasone/salmeterol in combination versus other inhaled steroids and bronchodilators alone. *COPD* 2007;**4**:127–34.

Lung alert

Selective proteasome inhibitors may provide a novel therapeutic approach to *Mycobacterium tuberculosis*

Proteasomes are large protein complexes that are structurally conserved across eukaryote cells including mycobacteria. They are needed to degrade unneeded or damaged proteins and, as such, have a vital role in cellular homeostasis. The cytotoxicity of proteasome inhibitors has been demonstrated by bortezomib (Velcade), which was the first therapeutic proteasome inhibitor and is licensed for use against multiple myeloma. Unfortunately, non-selective proteasome inhibitors are inherently toxic, limiting their potential use. In the present study the authors screened over 20 000 compounds to identify two oxathiazol-2-one inhibitors—GL5 and HT117—that were able to cross the cell wall of *Mycobacterium tuberculosis* and inhibit proteasome activity. These compounds were compared with bortezomib for efficacy and toxicity. Measured against the BCG strain, at equal concentrations GL5 and HT117 inhibited around 90% of mycobacterial proteasome activity compared with 52% achieved by bortezomib. Both compounds dose-dependently killed *M tuberculosis* over 4 days in synergy with nitric oxide (which at sub-lethal levels renders *M tuberculosis* non-replicative). Furthermore, GL5 and HT117 were non-toxic to mammalian cells when given at concentrations 3000-fold greater than those at which bortezomib killed monkey epithelial cells. In kinetic studies, oxathiazol-2-one compounds inhibited *M tuberculosis* proteasomes irreversibly.

Non-replicating *M tuberculosis* displays relative resistance to conventional antibiotics. Mycobactericidal, non-cytotoxic proteasome inhibitors that act irreversibly may provide a novel therapeutic tool against *M tuberculosis* as well as a synergistic adjunct to conventional anti-tuberculosis medications.

► **Lin G, Li D, Sorio de Carvalho LP, et al.** Inhibitors selective for mycobacterial versus human proteasomes. *Nature* 2009;**461**:621–6.

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