or syndrome of inappropriate antidiuretic hormone secretion (SIADH) in association with hypervolemic or euvolemic hyponatremia (serum sodium level <135 mmol/l). Patients received tolvaptan 15 mg daily for up to 30 days ($n = 102$ in SALT-1 and $n = 123$ in SALT-2) or placebo ($n = 103$ in SALT-1 and $n = 120$ in SALT-2). Doses were adjusted during the first 4 days to achieve a serum sodium concentration of at least 135 mmol/l.

From baseline to day 4, and from baseline to day 30, average daily increases in the area under the curve for serum sodium concentrations were significantly greater in tolvaptan-treated patients than in those receiving placebo ($P < 0.001$ for all comparisons). Absolute serum sodium level increases were also significantly greater in tolvaptan-treated patients ($P < 0.001$ for all comparisons). Hyponatremia recurred 1 week after tolvaptan discontinuation. On days 4 and 30 in both studies, more tolvaptan-treated patients than placebo recipients had normal serum sodium concentrations, and marked hyponatremia was more common in placebo recipients. On day 30, tolvaptan-treated patients showed improvement in mental component scores of a health questionnaire (when results from both trials were combined); physical component scores did not differ between groups. Thirst and dry mouth were the most common adverse events occurring in tolvaptan-treated patients. Overall, 14 tolvaptan-treated patients and 13 placebo-treated patients died.

Original article Schrier RW *et al.* (2006) Tolvaptan, a selective oral vasopressin V_2-receptor antagonist, for hyponatremia. *N Engl J Med* **355:** 2099–2112

Agalsidase beta slows the progression of advanced Fabry's disease

Fabry's disease results from a deficiency of the lysosomal enzyme α-galactosidase A; accumulation of this enzyme's substrates can cause renal, cardiac and cerebrovascular dysfunction, and lead to early death. In this paper, Banikazemi *et al.* report on a randomized, double-blind, placebo-controlled trial that investigated the effects of agalsidase beta (recombinant α-galactosidase A) on clinical outcomes in 82 adult patients with advanced Fabry's disease and mild to moderate kidney dysfunction.

The study took place from February 2001 to January 2004, and took the form of a time-to-first-event analysis of the composite end point of renal, cardiac or cerebrovascular events, or death. The FDA approved agalsidase beta in 2003 on the basis of results of studies of a surrogate marker, but required this further trial to demonstrate the drug's clinical benefit. Patients were infused with 1 mg/kg body weight agalsidase beta or placebo fortnightly for up to 35 months (mean 18.4 months). End-point events—mostly renal—were observed in 42% (13/31) of patients who received placebo, and in 27% (14/51) of the treatment group. Primary intention to treat analysis, adjusted for baseline proteinuria, revealed that agalsidase beta therapy increased the time to first clinical event compared with placebo (hazard ratio 0.47; $P = 0.06$).

The authors observe that patients with less-advanced Fabry's disease probably received the greatest clinical benefit from agalsidase beta. They also note that, although 61% of the treatment group and 32% of the placebo group experienced adverse events associated with the infusion therapy, only 3 of 56 serious adverse events were considered to be treatment-related.

Original article Banikazemi M *et al.* (2007) Agalsidase-beta therapy for advanced Fabry disease: a randomized trial. *Ann Intern Med* **146:** 77–86

Lowering blood pressure could protect against renal dysfunction in type 1 diabetes

Blood pressure (BP) control has been shown to offset the strong relationship between diabetes and the development of renal disease. A target BP of <130/80 mmHg is recommended for people with diabetes, but this is based largely on randomized controlled trials in patients with type 2 diabetes. Shankar and co-workers, therefore, investigated the relationship between BP and kidney function in people with type 1 diabetes.

A prospective population-based study of people with type 1 diabetes was performed over a 16-year period; most of the individuals enrolled had BPs within the low-normal range. As systolic and diastolic BP decreased, so did the relative risks of developing incident proteinuria ($P_{trend} = 0.03$ and $P_{trend} < 0.0001$ for decreasing quartiles of systolic [to a minimum