reductions were correlated with reductions in i-PTH levels ($r = 0.495; \ P = 0.024$). There were no relationships between IL-6 changes and the main mineral metabolism related parameters.

Our results agree with previous experimental findings [4] and point to the efficacy of calcimimetic drugs for the control of uraemic SHP.

It was unexpected that 6 months of cinacalcet treatment resulted in highly significant increases in OPG and decreases in Fetuin-A serum levels. OPG, a cytokine produced and secreted mainly by osteoblasts, has been claimed to play an as yet undefined role in the vascular calcification process. Although a protective effect of increased OPG levels on vascular calcification has been suggested, higher OPG serum levels have been linked to an increased extent of arterial wall calcification, increased mortality rates in uraemic patients, and most importantly, with increased mortality in dialysis patients [3,5]. The clinical significance of the OPG increase observed in our patients and its potential effects on the vascular calcification process cannot be drawn from our data. Interestingly, OPG increases were significantly correlated with the degree of reduction in c-Ca levels. In association with the OPG increases, cinacalcet treatment also caused significant decreases in Fetuin-A levels without changes in IL-6, indicating no change in the inflammatory state in our patients. The Fetuin-A reduction was significantly related to PTH decreases. Previous studies have emphasized an association between low Fetuin-A levels with both increased vascular calcification and cardiovascular mortality [2,6]. From our data, we cannot determine whether the Fetuin-A decrease represents a real increase in risk for the calcification process, or whether it is the consequence of a reduced demand for a feedback defence mechanism, which may be secondary to improved mineral metabolism, by cinacalcet, that reduces the pro-calcification burden. This possibility was proposed in non-dialysed diabetic nephropathy patients [7].

Although we are aware of the main limitation of this preliminary study, the highly significant changes in both OPG and Fetuin-A levels observed in our patients provide a stimulus and starting point for further research in this field.

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Conflict of interest statement. Dr Piergiorgio Messa received lecture fees from AMGEN, ABBOTT, and DOMPE’ BIOTEC. The other authors have no conflict of interest to declare.

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Does size matter?

Sir,

In the November 2006 issue of JASN, Opelz et al. published their analysis of the association of ACEI/ARB with patient and graft survival after renal transplantation utilizing the CTS registry [1]. In contrast to our study, published in JASN in March 2006, Opelz and colleagues reported that they failed to find such an association [2].

How can that be?

(i) There are differences in the group definitions and inclusion criteria between the two studies. While we included all patients transplanted between 1990 and 2003 with a functioning graft 3 months after transplantation, Opelz et al. used only patients transplanted between 1995 and 2004, with functioning graft 1 year after transplantation.

(ii) There are differences in the way ACEI/ARB enters the analysis. While we used ACEI/ARB intake as a time-dependent variable, and only for graphical illustration divided our patients into those who had received ACEI/ARB treatment after transplantation and those who had never received such treatment, Opelz et al. used ACEI/ARB in a fixed manner, comparing groups based on ACEI/ARB treatment at the time of 1 year after transplantation. In order to compare these results to ours, we performed a re-analysis of our database, including only patients transplanted from 1995 on and only those who had a functioning graft 1 year after transplantation. Then we used the same group definition as Opelz and colleagues and compared our new results to their and our published ones. We obtained the following survival curves (restricted to 6 years of follow-up, as in the publication of Opelz et al.) (Figure 1).

At 6 years of follow-up, the survival rates are comparable (Table 1).

We computed the crude (unadjusted for confounding) hazard ratio (HR) for ACEI/ARB use with the reduced data base, for graft and patient survival. These hazard ratio estimates compare to the results based on time-varying entry of ACEI/ARB use are displayed in Table 2.
The most striking difference between the two analyses lies in the way information on ACEI/ARB treatment was obtained. In the study of Opelz et al., a questionnaire was sent out, with a return rate of 107 out of 299 participating centres. Their publication does not provide information on how completely the data was collected within those 107 centres. By contrast, we used data bases from the general public Austrian Sickness Funds and direct entry from patient charts.

Furthermore, we included the confounding variables in a time-varying manner. Different strategies to identify confounding variables yielded virtually the same results. Finally, we did not explicitly recommend ACEI/ARB use, we rather encouraged the scientific community to test a potentially causal relationship between ACEI/ARB use and increased survival in a randomized controlled clinical trial.

Conflict of interest statement. None declared.

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**Effective treatment of four consecutive idiopathic membranous nephropathy patients**

Sir,

Idiopathic membranous nephropathy (IMN) is a common cause of nephrotic syndrome in adults. The course of this disorder is often benign; however, the disease progresses to end-stage renal failure at 10 years, in approximately one-third of untreated patients [1]. Although several therapeutic regimens, including corticosteroids and other immunosuppressive drugs, have been studied, their efficacy is highly debated. Thus, new drugs or regimens with a higher efficacy and fewer side effects are urgently required for treating high-risk IMN patients [2], such as those with persistent high-grade proteinuria. We previously reported the effects of treatment with mizoribine followed by low-dose prednisone in four IMN and nephrotic syndrome patients [3]. Mizoribine inhibits purine nucleoside synthesis [4], and it is administered to patients after kidney transplantation in Japan, because of its fewer side effects.

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![Graph](image-url)

**Table 1.** Survival rate at 6 years

<table>
<thead>
<tr>
<th>Group</th>
<th>Graft survival</th>
<th>Patient survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Our data</td>
<td>Opelz et al.</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>85.5%</td>
<td>82.5%</td>
</tr>
<tr>
<td>No ACEI/ARB</td>
<td>80.8%</td>
<td>83.7%</td>
</tr>
</tbody>
</table>

**Table 2.** Cox proportional hazard regression models

<table>
<thead>
<tr>
<th>Mode of analysis</th>
<th>Graft survival HR (95% confidence interval)</th>
<th>Patient survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time-varying (Heinze et al.)</td>
<td>0.76 (0.64–0.90)</td>
<td>0.70 (0.58–0.86)</td>
</tr>
<tr>
<td>Fixed at 1 year (Opelz et al.)</td>
<td>0.70 (0.48–1.02)</td>
<td>0.80 (0.52–1.24)</td>
</tr>
</tbody>
</table>