Correspondence

Long-term cost-efficacy of rituximab in immune thrombocytopenic purpura

Sir,

Prior to 1981, the only effective treatments for increasing platelet count in immune thrombocytopenic purpura (ITP) were corticosteroids and splenectomy. More recently, intravenous immunoglobulin (IVIg) and Rh immunoglobulin (IV RhIg) have demonstrated efficacy. Other treatments, including danazol, azathioprine, cyclophosphamide, vinca alkaloids and cyclosporin A, are supported by small and mostly uncontrolled clinical trials.

When conventional therapy fails, ITP may be a challenging clinical situation, as long-term corticosteroids have severe side-effects, and IVIg loses its efficacy over the long term. Monoclonal antiCD20 antibodies (rituximab) appear to be effective in ITP, but controlled clinical trials are lacking.1 We present a case of refractory ITP with a sustained response to rituximab, and discuss the cost/benefit ratio of other therapies in relation to this case.

In 1996, a 37-year-old White male patient was admitted to our Department with low platelet count (5000 platelets/mm$^3$) and purpura on his feet. He had been transfused several years earlier following an accident. He denied alcohol or drug consumption. Blood count showed normal red and white cells. AST and ALT were increased (x2), HCV serology and RNA were positive, and a liver biopsy showed active chronic hepatitis. He was given prednisone (1 mg/kg), with a good response. Due to concern about the progression of liver damage, we administered $a$-interferon in 1996 but had to be discontinued after exacerbation of thrombocytopenia and thyroiditis. Between 1996 and 1998, he suffered several bouts of ITP, all treated with corticosteroids. Splenectomy was performed in July 1998. Seven months later, he relapsed, with extreme thrombocytopenia. From 2001 to 2003, his ITP became refractory to corticosteroids, and IVIg was used. In February 2003, we administered rituximab (Mabthera, Roche) 375 mg/m$^2$ i.v. once weekly for 4 consecutive weeks. Rituximab was well tolerated. Platelet counts remained normal until August 2005 (29 months), when he suffered a new bout of thrombocytopenic purpura (1000 platelets/mm$^3$), again treated with prednisone and IVIg.

Given the sustained response of his thrombocytopenia (29 months), issues arise not only of efficacy but of cost-efficiency as well. We may consider two periods of time in this case: from 1996 to 2003 (55 months) and from 2003 to 2005 (29 months). During the first period, the patient had eight hospital admissions, underwent splenectomy, and was seen at our out-patient clinic 41 times. During the second period, after rituximab, no admissions were recorded, and he visited the clinic 5 times. We estimate costs at approximately 46 200 Euros during the first period, and 12 200 Euros for the second period, with no account taken of patient’s travel costs or discomfort. These figures represent costs of 840 Euros and 420 Euros per month, respectively. According to this data, rituximab seems to be more cost-effective than standard therapy for refractory cases, as it allowed a reduction of 50% of direct costs.

A second concern relates to the safety of immunosuppressant drugs in patients with underlying viral illnesses, as in this case. During the first period, we administered prednisone, either alone or combined, with one of the following: cyclophosphamide, cyclosporine or azathioprine. Furthermore, from 1997 to 2001, liver histology evolved from chronic active hepatitis to cirrhosis. Rituximab was well tolerated, and no signs of liver decompensation or disease progression were seen.2

Rituximab appears to be safe and well tolerated, and about 50% of patients with ITP respond to it.1 Accordingly, it can be a good alternative for patients in whom corticosteroid therapy fails in controlling thrombocytopenia. Indications for splenectomy,
IVIg and other immunosuppressant drugs should probably be revisited.

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Religious believers and strong atheists may both be less depressed than existentially-uncertain people

Sir,
Although controversial, it is often argued that religious belief is a cause of greater happiness.1 However, we have found in two separate studies that both theism and atheism are correlated with fewer reported depressive symptoms than the in-between state of ‘existential uncertainty’.

In our first study, on the effect of religious conviction on the Beck Depression Inventory (BDI), there was an unanticipated ‘inverted-U’ relationship, where the most and least religious groups had fewest depressive symptoms. In the second, we devised an 11-item existential conviction scale (ECS) as a measure of the degree of human life [http://www.hed-web.com/bgcharlton/ecsq]. Fifty-two subjects (24 male, 28 female; age 18–76 years) completed the ECS and BDI. All 10 of those who rated as depressed (‘mild’ depression, BDI score 10+) were roughly halfway between atheist and theist. There was a significant negative relationship between ECS and the BDI (Spearman rank correlation −0.44, p < 0.2).

There are several plausible explanations for such an association. Most obviously, strong beliefs may protect against depression, or conversely, low mood may diminish strong beliefs. Alternatively, depressive symptoms and existential uncertainty may both be a consequence of confounding by systemic illnesses, because immune activation tends to cause malaise symptoms such as fatigue (leading to depressed mood) and impaired concentration (perhaps leading to greater uncertainty of beliefs).2–4 This hypothesis is currently being tested.

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Why do older patients die in a heatwave?

Sir,
I was interested in the recent Commentary by Flynn, McGreevy and Mulkerrin,1 which contained some thoughts on why elderly people are vulnerable in a heat wave.

However, they did not mention the important confounding factor of elevated ambient ozone levels, which commonly occur at the same time as the heat wave. Recent reports2–4 have suggested that a significant proportion of the additional deaths in recent heat waves might well be due to elevated tropospheric ozone. This extremely irritant gas causes changes in the lungs that might very well be dangerous to those with congestive heart failure or other circulatory conditions.

The authors noted that others have recommended the opening of windows as a precautionary measure. This reminded me that when I was a