Letters

Stopping a medical research project for financial reasons

SIR,

We are writing to provide some clarifications on the Editorial Comment by Dru¨eke et al. [1]. We would have been happy to provide these very same clarifications had we been fairly invited to do so before the publication of the article.

First of all, we would like to underline that cancelling a clinical trial is always a difficult and costly decision for any pharmaceutical company, for many reasons. In the case of the clinical trial mentioned in Dru¨eke et al. [1], we acknowledge and are convinced that there were several indications of possible benefits of NAC in ESRD patients. The trial we stopped was only a preliminary exploratory study to be followed by larger pivotal clinical trials with hard clinical endpoints, as required by Regulatory Authorities. After a thorough re-examination of the clinical development plan, Zambon considered that the regulatory constraints it faced required a thorough re-examination of the clinical development plan, rather than any conduct was perpetrated. Furthermore, all the participating investigators were promptly informed of the decision suspending the trial were provided.

In reference to the comment by Dru¨eke et al. [1] about the implications of interrupting a clinical trial, Zambon took special care to ensure that the trial was stopped before any patient had received the study medication, thus avoiding possible harm to the patient’s health condition or to his/her expectations. In this regard, we wish to point out that the status of the trial, at the time it was interrupted, was as follows. (i) Only part of the study sites had received approval from the Ethics Committee. (ii) Only 3 out of 40 study sites had received the initiation visit, thus being officially authorized to start enrolling patients. (iii) The study drug had not yet been distributed to any of the study sites. (iv) Only three patients in a single study site had signed the informed consent, but no one of them had undergone any study procedure. Accordingly, in our opinion, no infringement of any conduct was perpetrated. Furthermore, all the participating investigators were promptly informed of the decision following a letter distributed by Zambon, where the reasons for suspending the trial were provided.

In conclusion, Zambon believes that all the actions required to interrupt the trial were performed in the most correct way, although it recognizes the distress that this decision may have caused to the parties involved.

Last but not least, the scientific community must well understand that the pharmaceutical industry has been hit in the last few years, practically in every country, by a wide array of cost-cutting measures that have severely affected margins and, in turn, the possibility of sustaining all preconceived R&D programs. At the same time and with similar scope, registration procedures everywhere are becoming more costly, lengthy and cumbersome. These factors cannot be overlooked since they will continue to generate disappointment in years to come.

Conflict of interest statement. C. Di Padova is currently the Director of the Research and Development Department of Zambon Group.

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DOI: 10.1093/ndt/gfh092

Detecting ‘decoy cells’ by phase-contrast microscopy

SIR,

A recent paper by Fogazzi et al. [1] shows how decoy cells can be identified not only by Papanicolaou stain on fixed urine or by immunocytochemistry, but also by phase-contrast microscopy without any stain.

BK Polyomavirus is a double-stranded DNA virus belonging to the Papovavirus family, and infects up to 90% of the general population. After primary infection, generally occurring in childhood without evident symptoms, the virus can remain latent in the urinary tract. Reactivation can be enhanced by immunosuppressive conditions, leading to overt clinical disease [2]. The most important clinical manifestations are haemorrhagic cystitis in bone marrow transplantation, ureteral stenosis and interstitial nephropathy in kidney transplant recipients [3].

BK virus nephropathy (BKN) has been identified as a frequent complication affecting renal transplantation recipients, possibly associated with the degree of immunosuppression, and leading to allograft dysfunction in ~50% of patients [4,5].

Histopathology is the gold standard test for diagnosis. Surrogate markers, such as detection of Polyomavirus-inclusion bearing cells (decoy cells) in the urine [6] and quantification of BK virus DNA in the plasma by polymerase chain reaction (PCR), have been used for diagnosis and management of polyomavirus BKN [7]. The presence of decoy cells in the urine is a 100% sensitive sign of elevated BK virus replication in the urogenital tract, but the positive predictive value for BKN may be <20%. Decoy cells are not exclusive to the BK virus. If PCR for BK virus is negative in urine specimens with presumed decoy cells, this does not exclude the presence of other viruses such as JC virus [8], and certain adenoviruses (e.g. type 11). Detection of BK virus DNA in plasma suggests significant allograft involvement (sensitivity 100%, specificity 88%) [5].

We confirm the results of the authors, reporting the case of a 61-year-old man, who received a kidney transplant in July 2002 from a cadaveric donor. In October 2002, his serum creatinine was 2.0 mg/dl, which then progressively increased up to 6.0 mg/dl in June 2003, while the patient was treated with tacrolimus and mycophenolate mofetil.

The urinalysis by phase-contrast microscopy showed ~2 decoy cells/high-power field, at ×400 (tubular and ureoepithe-