Beyond these insights there are further applications and future challenges

Sir,

Insights into the genetic susceptibility to Crohn’s disease (CD)\(^1\) would be incomplete without recognition that the unrivalled success of azathioprine in inducing and maintaining remission in corticosteroid-dependent CD\(^2\) ought to go hand in hand with a wider application of pharmacogenetic testing\(^3\) so as to optimize efficacy and safety of this agent. The rationale for pharmacogenetic testing is that polymorphism at the gene locus for thiopurine transmethylase (TPMT) is the operative mechanism for determining tissue levels of this enzyme and, hence, the degree to which any individual patient might be at risk of myelosuppression attributable to suboptimal inactivation of azathioprine by TPMT.\(^2\) However, notwithstanding the human and financial cost of inadvertent myelosuppression, in a national survey of consultant gastroenterologists, dermatologists and rheumatologists, where the response rate was 70%, only 60% of gastroenterologists reportedly tested their patients for TPMT activity before prescribing azathioprine.\(^3\) Suboptimal TPMT testing might be attributable to insufficient recognition that pharmacogenetic tests not only offer patient benefits but also ‘have an impact on finite healthcare resources’\(^4\). The latter is a principle also translatable to cancer management, where pharmacogenetic testing has the potential, not only to identify individuals predisposed to a high risk of toxicity and low response from standard doses of anticancer drugs\(^5\), but, arguably, also to predict which patients will achieve a good therapeutic response without experiencing severe side effects. For example, had pharmacogenetic profiling been part of the strategy for evaluating the cost-effectiveness of temsirolimus, the chemotherapeutic agent for advanced renal cell carcinoma, instead of the evidence presented to National Institute for Health and Clinical Excellence being ‘convincing [only] for the overall data but not for the subgroup data’,\(^6\) subgroups might have emerged with benefit vs. risk profiles so favourable as to relegate drug costs to lower priority, thereby justifying inclusion of this drug in the National Health Service therapeutic armamentarium.

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