Reply to: About the AIRTRIP randomised clinical trial

Sirs,

We thank Drs Dincses and Seyahi for their interest in our work (1, 2), which gives us the opportunity to further expand some points.

The current status of the medical literature is that a case series, even if prospective, is inevitably labelled with a low C level of evidence, based on case series and expert opinion. In this setting, it becomes difficult even to obtain the active drug to administer to the patients, since both hospitals and drug companies are reluctant to give it. On the other hand, a randomised controlled trial (RCT) is graded as an A class of evidence, and considered as the gold standard. This is also justified by the fact that a RCT by definition necessitates a rigid protocol. For instance, our protocol mandated a quick tapering of all the drugs, except colchicine, within 6 weeks. We agree that anakinra has a spectacular effect when used in the correctly selected patients, but only a RCT has the strength to demonstrate this in the modern era. This issue is completely unrelated to drug licensing. This study was investigator-initiated. SOBI provided anakinra and placebo as part of an unrestricted institutional grant, and had no role in the design and conduct of the study and in the preparation of the manuscript. SOBI is currently evaluating the outcomes of this study and potential next steps.

We used a withdrawal design consisting of 2 parts: an open-label treatment period in which anakinra was administered daily for 60 days, followed by a double-blind withdrawal period, in which patients who had a sustained complete response in part 1 were randomised to receive anakinra or placebo daily for up to 6 months. This design was aimed to minimise the exposure to placebo (3); this method was similarly used to demonstrate the efficacy of anakinra in the cryopyrin-associated periodic syndromes (4). Theoretically, it would select responding patients, but in practice we had the situation in which ALL the patients had a complete sustained response to the active drugs, and all of them entered the second double-blind withdrawal phase. The possible enrichment of a population with responders in the second phase is a theoretical concern, but not applicable to this specific study.

Even if the original proposal to treat patients with colchine-resistant and steroid-dependent recurrent pericarditis with anti-IL1 treatment come from the paediatric experience of treating children with autoinflammatory disorders, it was clear to us that the vast majority of patients in real life are adults. For this reason only one patient included in our study was in the paediatric age range (15 years old) and the remaining 20 patients were adults (aged >18 years). The paediatric patient was enrolled at the Gaslini Paediatric Insitute, while the other 20 adults patients were enrolled in Torino and Bergamo referral centres mainly devoted to the care of adults with pericarditis (Torino is a cardiological centre, and Bergamo is an internal medicine centre).

In our study colchicine resistance indicated that all the patients continued to suffer recurrences despite colchicine therapy, and we think that this is clearly brought up in our paper.

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the other authors have declared no competing interests.

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