Autologous stem cell transplantation with low-dose cyclophosphamide to improve mucosal healing in adults with refractory Crohn's disease: the ASTIClite RCT

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Plain language summary

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Background

Crohn's disease occurs when the gut immune system reacts to its bacterial content, causing bowel inflammation. For some patients, standard treatments for Crohn's disease are ineffective, leading to debilitating symptoms, poor quality of life and the possibility of operations that can result in a stoma. Initial reports suggested that treatment-resistant Crohn's disease could be improved with stem cell transplantation (haematopoietic stem cell transplant), whereby a patient's own immune stem cells are returned to them after their current immune system is wiped out by chemotherapy.

Objectives

The ASTIClite trial aimed to test HSCT with low-dose chemotherapy (HSCTlite) to investigate whether or not this could be a safe and effective treatment for Crohn's disease. The ASTIClite trial also looked at how HSCT works.

Methods

The ASTIClite trial was a randomised controlled trial that aimed to recruit 99 patients with treatment-resistant Crohn's disease, across eight UK NHS centres. Patients were followed up every few weeks, and at 48 weeks we assessed whether or not HSCT was more likely to lead to healing of intestinal inflammation than standard care. Some patients experienced severe side effects, and the trial was closed early after 23 patients were recruited in view of the reported issues with the safety of the trial treatment.

Results

Because the trial was stopped early, 23 patients joined ASTIClite (HSCT arm, $n = 13$; usual-care arm, $n = 10$), which was a much lower number than originally planned. At 48 weeks, three out of seven HSCT patients had absence of ulceration, with zero out of six in the usual-care arm having absence of ulceration. Three out of six HSCT patients had disease remission, compared with zero out of three usual-care patients. All patients in the HSCT arm experienced at least one side effect ($n = 38$ serious side effects in total), and two patients died. In the usual-care arm, 4 out of 10 patients experienced adverse events ($n = 16$ serious adverse events in total).

Conclusions

Although firm conclusions are not possible because of the limited numbers of patients recruited before trial closure, it does appear that HSCT using the ASTIClite regimen reduced Crohn's disease activity in some patients. However, the numbers of serious and unexpected side effects mean that this treatment plan would be unsuitable for future clinical use.

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