2024. ASTIClite

RCT/HSCT /refractory CD/Endoscopic rem

Safety and efficacy of autologous haematopoietic stem-cell transplantation with low-dose cyclophosphamide mobilisation and reduced intensity conditioning versus standard of care in refractory Crohn's disease (ASTIClite): an open-label, multicentre, randomised controlled trial

Open-label multicentre, randomised controlled trial. Adults with active CD on endoscopy refractory to 2 or more biologicals with no perianal or intra-abdominal sepsis or significat comorbidity were recruited. Patients were randomised to HSCT (hematopoietic stem-cell transplantation) with a reduced dose of cyclophosphamide or standard available care (control group)

Patients in the intervention group underwent stem-cell mobilisation (cyclophosphamide 1 g/m^2 with granulocyte colony-stimulating factor (G-CSF) 5 µg/kg) and stem-cell harvest (minimum 2·0 × 10^6 CD34+ cells per kg), before conditioning (fludarabine 125 mg/m^2, cyclophosphamide 120 mg/kg, and rabbit anti-thymocyte globulin [thymoglobulin] 7·5 mg/kg in total) and subsequent stem-cell reinfusion supported by G-CSF.

<u>Primary endpoint</u>: Absence of endoscopic ulceration (SES-CD ulcer sub-score of 0) without surgery or death at w48

<u>Results: N=23</u> (Study was halted in response to serious AEs)

- Severe AEs in the intervention group: renal failure due to thrombotic microangiopathy (n=3), 1 death due to pulmonary veno-occlusive disease, 1 death due to respiratory and renal failure
- At w48 endoscopic improvement with no surgery/death was 43% (3/7) vs none in control group.

<u>Conclusion:</u>

Although HSCT with an immune-ablative regimen of reduced intensity decreased endoscopic disease activity, significant adverse events deem this regimen unsuitable for future clinical use in patients with refractory CD.

	Mobilisation		Transplantation		Follow-up		Total*
	Intervention group (n=13)	Control group (n=10)	Intervention group (n=13)	Control group (n=10)	Intervention group (n=13)	Control group (n=10)	Intervention group (n=13
Number of participants with ≥1 SAE	2 (15%)	2 (20%)	11 (85%)	3 (30%)	6 (46%)	3 (30%)	13 (100%)
Number of all SAEs (including repeated events)	4	3	24	3	8	9	38
Number of SAEs by seriousness							
Death	0	0	1	0	0	0	1
Life-threatening	1	0	3	1	0	0	4
Inpatient hospitalisation	3	3	10	2	6	9	21
Extended hospitalisation	0	0	3	0	2	0	5
Persistent or clinically significant disability or incapacity	0	0	3	0	0	0	3
Congenital abnormality or birth defect	0	0	0	0	0	0	0
Another important medical event	0	0	4	0	0	0	4
Number of SAEs by outcome							
Recovery	3	1	11	2	2	2	17
Improvement	1	2	7	1	3	7	12
No change	0	0	3	0	1	0	4
Deterioration	0	0	0	0	0	0	0
Persistence	0	0	0	0	1	0	1
Death†	0	0	3	0	1	0	4

Data are n (%) or n. SAE=serious adverse event. *Includes all SAEs, including those that occurred before mobilisation, hence the discrepancy between total SAEs and the sum

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