

Ciclosporin blood levels and clinical outcomes in obese bone-marrow transplant patients after weight-based dosing

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BACKGROUND

- Ciclosporin (CSA): Commonly used calcineurin inhibitor in Haematopoietic stem cell transplantation (HSCT)
- Initiated as weight-based loading and maintenance doses → then adjust with Therapeutic Drug Monitoring (TDM)
- Not clear whether **Actual** body weight, **Ideal** body weight or **Adjusted** body weight should be used to calculate initial CSA doses in obese patients.

AIM

Investigating the appropriateness of using **Actual** body weight when calculating CSA doses in obese patients by;

- Comparing CSA trough levels between obese and non-obese patients after **Actual** body weight based initial dosing.
- Evaluating clinical outcomes : Acute Kidney Injury (AKI:CDIGO criteria) and acute graft-versus-host disease (aGVHD).

METHODS

Study design

A single centre retrospective cohort study comparing the endpoints between obese (weight > 120% Ideal body weight) and non-obese patients

Patients

Inclusion criteria: Patients who had FluMel or CyTBI allogeneic HSCT between 2017 and 2020 with initial CSA based on **Actual** body weight

Exclusion criteria: Initial CSA based on **Ideal** or **Adjusted** body weight, or concurrent strong CYP3A4/5 inhibitors or inducers

Treatment

- CSA loading dose 5mg/kg IV daily → 3mg/kg IV daily then adjust with TDM
- Target trough levels:120-300 mcg/L (whole blood HPLC)
- Methotrexate 15mg/m² day +1, 10mg/m² Days 3,6 &11

Data collection

Demographics, Cr, CSA levels, aGVHD

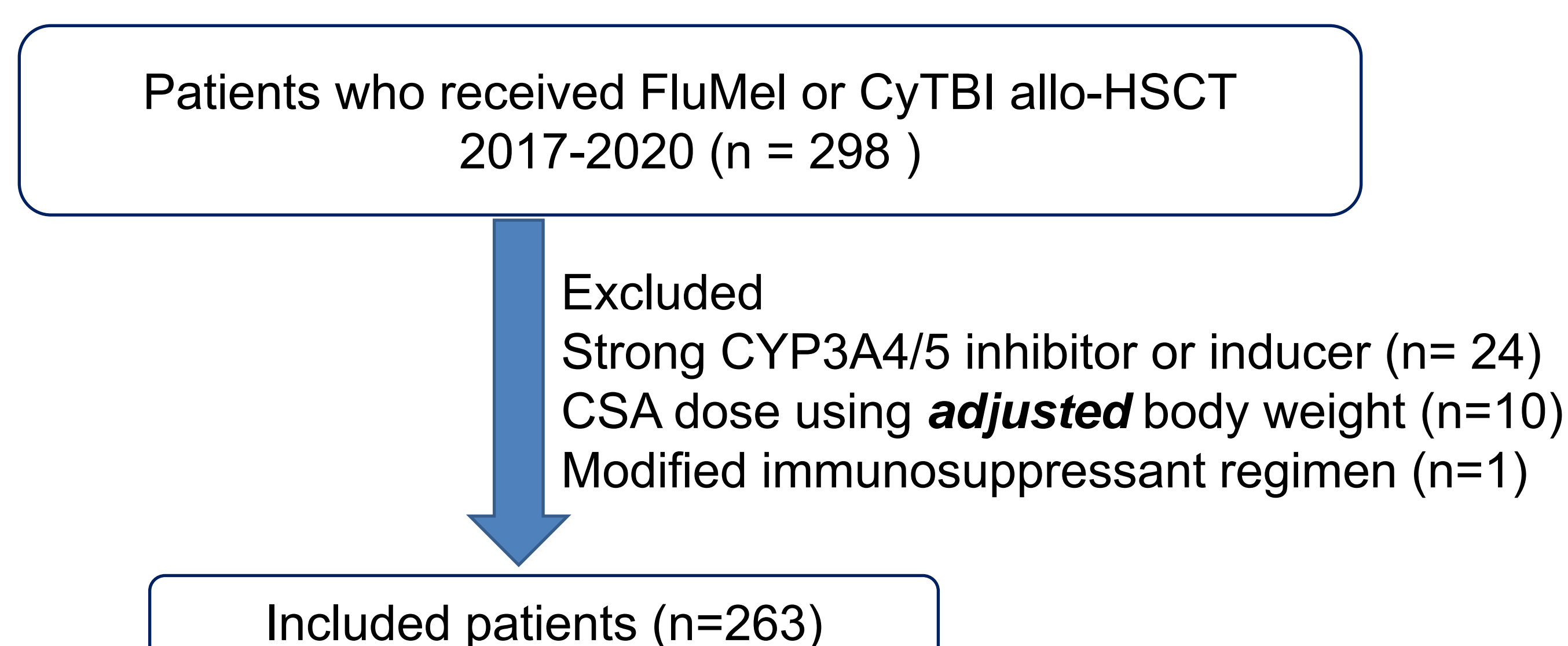
Study endpoints

- CSA trough levels
- Incidence and grades of AKI
- Incidence and grades of aGVHD

Data analysis: Student t-test and Chi Squire test

RESULTS

Patients



RESULTS continued

Patients' characteristics : Similar except weight

	Non-Obese	Obese
Number of patients	145	118
Female	56 (39%)	50 (42%)
Median age (years)	57	54
Age range (years)	18-74	18-74
Mean height (cm)	172.8	172.5
Mean weight (kg)	71.5	93.3
Flu-Mel conditioning	106 (73%)	82 (70%)
Cy-TBI conditioning	39 (27%)	36 (30%)
Mean baseline creatinine (mmol/L)	71	73

CSA trough levels: Significantly high in obese patients

	Non-obese (n=145)	Obese (n=118)	
Mean initial CSA level (mcg/L)	187	237	p=0.001
Mean CSA level #1-3 (mcg/L)	182	224	P<0.001
Mean CSA level pre-engraftment (mcg/L)	189	220	P<0.001
Number of patients with initial CSA > 300mcg/L	9 (6%)	18 (15%)	p=0.028
Number of patients with CSA level #1-3 >300mcg/L	16 (11%)	31 (26%)	p=0.002

Incidence of AKI: No significant differences

	Non-Obese (n=145)	Obese (n=118)	
Total AKI	36 (25%)	36 (31%)	p=0.33
Stage I	22 (15%)	21 (18%)	
Stage II	10 (7%)	11 (9%)	
Stage III	4 (3%)	4 (3%)	
Mean (Maximum Cr/ Baseline Cr)	1.357	1.449	p=0.187

Incidence of acute GVHD:

Significantly higher in obese patients despite higher CSA levels

	Non-Obese (n=145)	Obese (n=118)	
Total aGVHD (all grades)	73 (50%)	77 (65%)	p=0.02
Grade 1	36 (25%)	30 (25%)	
Grade 2	24 (17%)	33 (28%)	
Grade 3	13 (9%)	14 (12%)	
Grade 4	0	0	

CONCLUSIONS

- When using **Actual** body weight based CSA dose, trough levels were higher in obese patients
- The higher CSA level did not significantly affect AKI.
- Despite higher CSA levels, obese patients had significantly higher incidence of aGVHD: Obesity is an independent risk factor
- Using **Actual** body weight appears to be safe – Closer monitoring may be required in obese patients