RUXOLITINIB AS SALVAGE THERAPY IN PEDIATRIAC PATIENTS WITH STEROID-REFRACTORY GRAFT-VERSUS-HOST DISEASE

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Background:

Steroid-refractory graft-versus-host disease (GVHD) is a significant complication of allogeneic hematopoietic stem cell transplantation (HSCT) and a leading cause of morbidity and non-relapse mortality.

Adult clinical trials with ruxolitinib have demonstrated benefit in this population, but there are no paediatric reports describing this effectiveness.

Purpose:

To analyze effectiveness and safety of ruxolitinib in pediatric patients, with steroid-refractory GVHD.

Material and methods:

Retrospective study including patients diagnosed of GVHD treated with ruxolitinib; from January 2017 - October 2018. Demographic and clinical data were collected from electronic medical records and Pharmacy software: sex, age, weight, type, location and severity of GVHD, previous treatments, dosing, duration of treatment, response and toxicities.

Results:

7 patients were included, 5 boys and 2 girls, with a median age of 11 years (5-18); and a median weight of 40kg (15-63). 2 patients developed acute GVHD (aGVHD) and 5 chronic GVHD (cGVHD). The median number of affected organs per patient was 3 (1-4): skin (n=6), gastrointestinal tract (n=5), lungs (n=4), joints (n=2), and liver (n=1).

Median number of treatments used before ruxolitinib was 4 (2-5), always including corticosteroids as the first option. Treatments in second or third line were: extracorporeal-photoapheresis, mesenchymal stem cells, immunosuppressants and infliximab.

Patients	Weight	Initial dose	Final dose
n= 3	> 25 kg	5 mg/12h	10 mg/12h
n= 2		10 mg/ 12h	10 mg/12h
n=1	< 25 kg	2,5 mg/12h	5 mg/12h
n=1		1,2 mg/12h	5 mg/12h

One patient started at a lower dose (1.25mg/12) because was in treatment with posaconazol.

The median treatment's duration was 10 months (3-19). All cGVHD were still in treatment at the end of the study

All patients responded to ruxolotinib: all patients with aGVHD had complete response and two patients with cGVHD had complete response (CR), and the remainder had partial response (PR).

GVHD type	Organs affected	Response	Organ without response
moderate chronic	skin, GI tract, joints, lungs	PR	joints
	skin, GI tract, joints, lungs	PR	joints
	skin	**CR**	
	skin, lungs	PR	skin
	skin, GI tract, lungs	**CR**	
acute grade III	GI tract	**CR**	
acute grade IV	skin, GI tract, liver	**CR**	

Digestive, cutaneous, lungs and liver symptoms showed improvement while GVHD affecting joints did not.

No patient died during the study. Only 2 patients presented leukopenia and 2 suffered reactivations of cytomegalovirus, but there was no dose reduction due to toxicity.

Conclusions

In our patients Ruxolitinib has proven to be an effective and safe treatment option, but well-designed clinical trials are necessary to know its real benefit in pediatrics patients with steroid-refractory GVHD.

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