



# Real World Evidence of the use of Defibrotide for prophylaxis of Veno-Occlusive Disease after post-haematopoietic stem-cell transplantation in children

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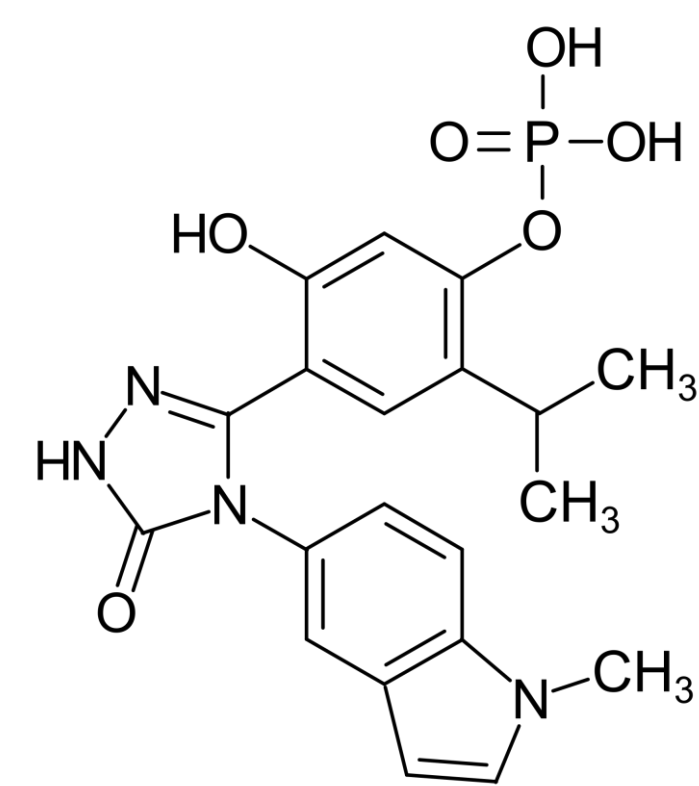
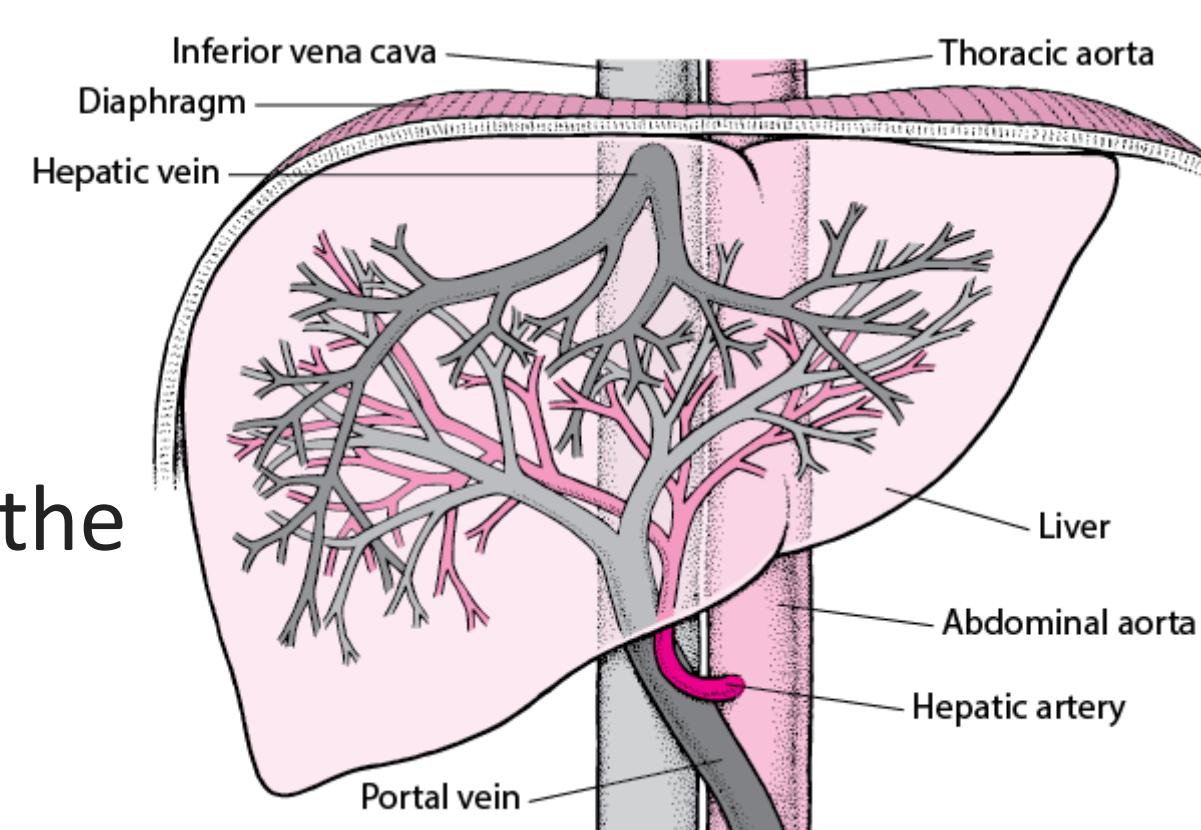
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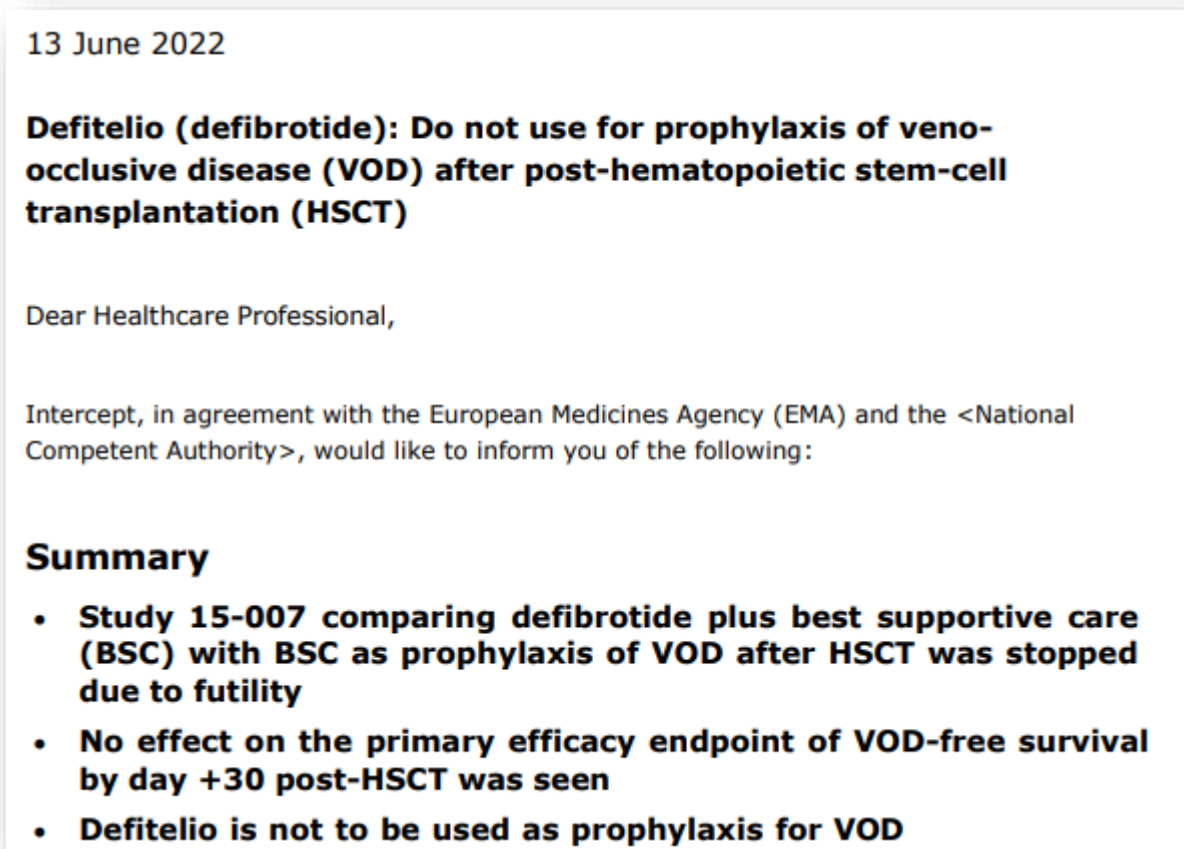
## BACKGROUND

**Hepatic Veno-Occlusive Disease (VOD)** is a life-threatening condition caused by the obstruction of liver sinusoids (1).

Since 2014, in Italy the standard of care for the management of VOD is represented by **defibrotide**.



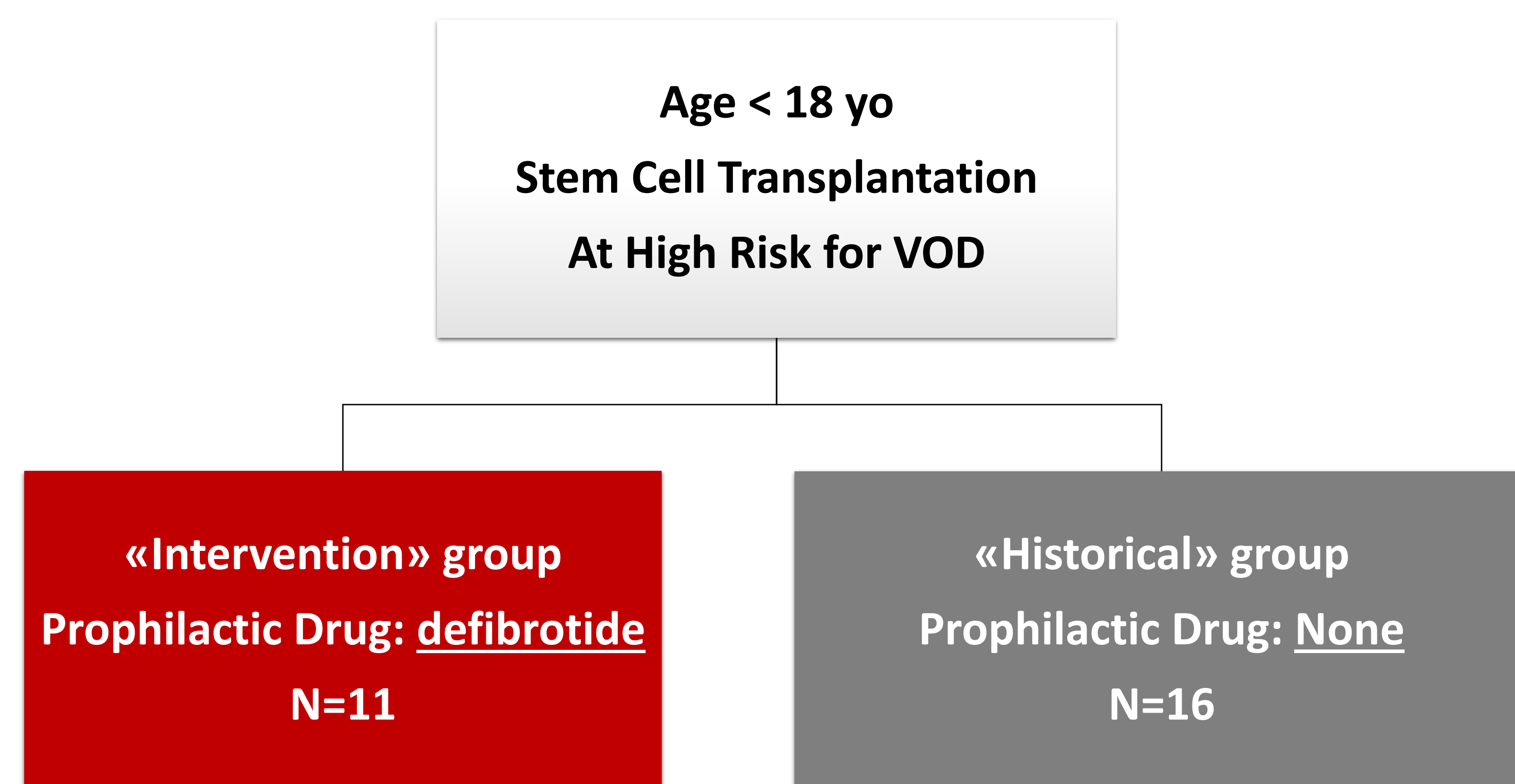
Recent evidence suggested that defibrotide could help preventing the onset of hepatic VOD when allogeneic hematopoietic stem cell transplantation is needed. On June 2022, however, a **“direct health professional communication”** issued by the **European Medicines Agency (EMA)** invoked not to use defibrotide anymore for VOD prophylaxis due to lack of effectiveness (2).



## MATERIAL AND METHODS

A **single-centre, retrospective study** was conducted at our University Hospital. All data were collected from electronic health records. These data were cross-checked with data from an integrated analytics application (Qlikview®, QlikTech International AB, King of Prussia, USA).

All **pediatric patients** (age <18 years) **undergoing hematopoietic stem cell transplantation for onco-haematological diseases and considered at high-risk for developing VOD** were enrolled.



## AIM AND OBJECTIVES

The aim of this work is to explore the **difference in the incidence of VODs at 30 days in 2 groups of children, with and without prophylaxis therapy with defibrotide before undergoing hematopoietic stem cell transplantation.**

## RESULTS

### BASELINE CHARACTERISTICS ACCORDING TO PROPHYLAXIS TREATMENT

Between 2020 and 2022, data were collected from 27 patients.

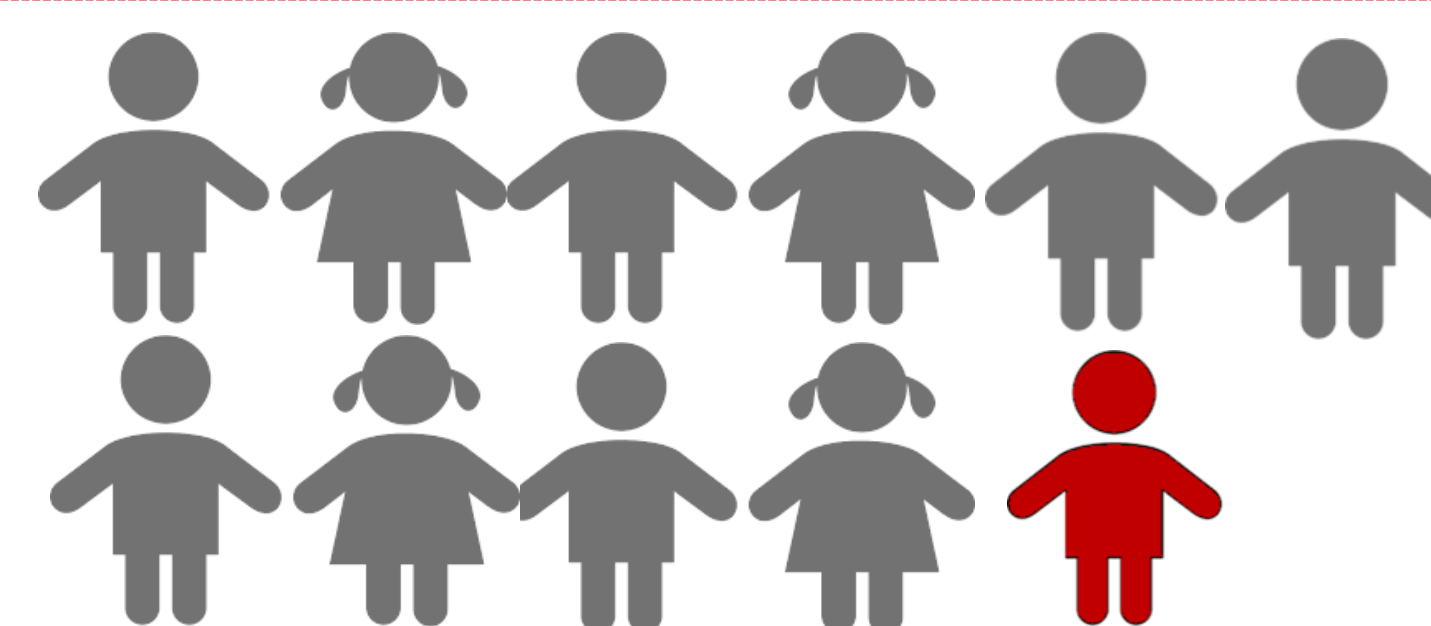
	Overall, N = 27 <sup>1</sup>	Historical Group, N= 16 <sup>1</sup>	Defibrotide, N = 11 <sup>1</sup>	p-value <sup>2</sup>
<b>Age</b>	9.0 (7.0, 12.5)	9.0 (7.0, 13.2)	9.0 (7.0, 12.0)	>0.9
Age(<=2 yo)				>0.9
Age >2	23 (85%)	14 (88%)	9 (82%)	
Age<=2	4 (15%)	2 (12%)	2 (18%)	
<b>Gender</b>				>0.9
Female	10 (37%)	6 (38%)	4 (36%)	
Male	17 (63%)	10 (62%)	7 (64%)	
<b>Haematological Disease</b>				0.5
Aplastic Anemia	2 (7.4%)	2 (12%)	0 (0%)	
Acute lymphoblastic leukemia	12 (44%)	6 (38%)	6 (55%)	
Acute myeloid leukemia	5 (19%)	2 (12%)	3 (27%)	
Hodgkin lymphoma	2 (7.4%)	2 (12%)	0 (0%)	
Ewing Sarcoma	2 (7.4%)	2 (12%)	0 (0%)	
Other	4 (15%)	2 (12%)	2 (18%)	
<b>Conditions determining a very high-risk</b>				0.4
No	26 (96%)	16 (100%)	10 (91%)	
Yes	1 (3.7%)	0 (0%)	1 (9.1%)	
Very high-risk patients	5 (19%)	2 (12%)	3 (27%)	0.4

<sup>1</sup>Median (IQR); n (%)

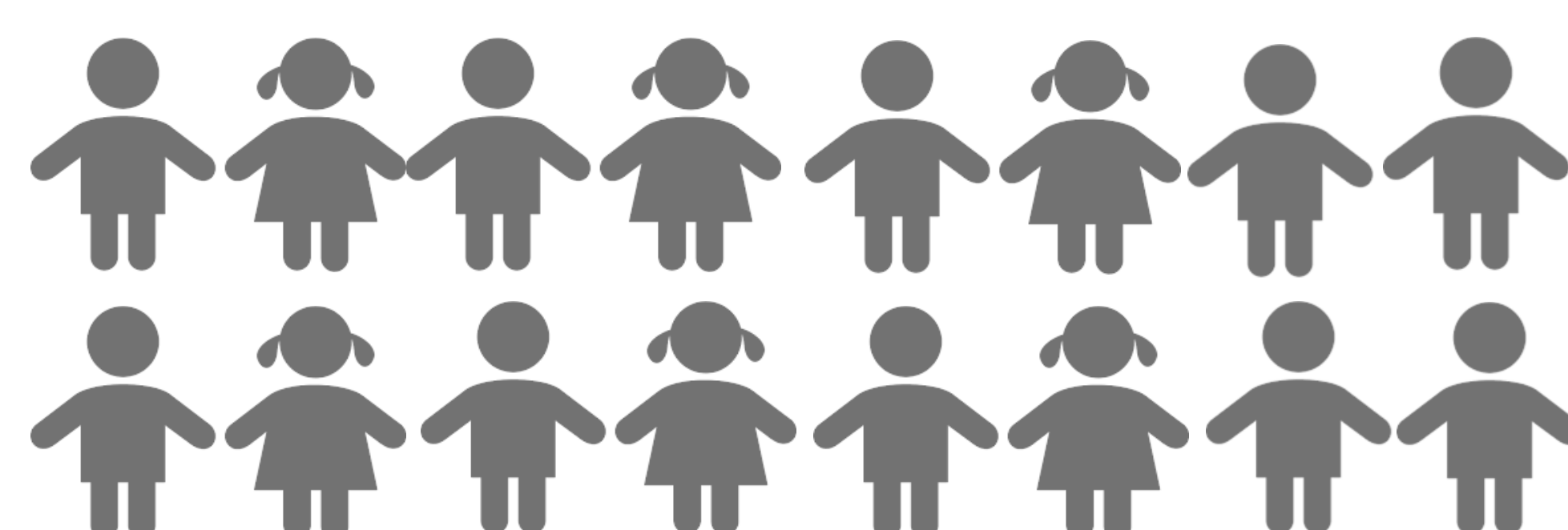
<sup>2</sup>Wilcoxon rank sum test; Fisher's exact test

### OUTCOMES

In terms of outcome, we witnessed only one episode of VOD, in the treatment group (1 of 11 patients, 9%), at 30 days after transplantation. No episodes were documented in the controls.



**INTERVENTION GROUP**  
**DEFIBROTIDE**  
 1/11 VODs (9%)  
 0/11 Deaths (0%)



**HISTORICAL GROUP**  
 0/16 VODs (0%)  
 0/16 Deaths (0%)

P=0.4

## CONCLUSION AND RELEVANCE

According to the recent statement made by the EMA, our data – although not definitive – show that **the proportion of VOD in children undergoing blood stem transplantation who received a prophylaxis treatment with defibrotide was comparable with the one in children where no prophylaxis strategy has been adopted.**

## REFERENCES

- Senzolo, M.; Germàni, G.; Cholongitas, E.; Burra, P.; Burroughs, A. Veno Occlusive Disease: Update on Clinical Management. *World J Gastroenterol* 2007, 13, 3918–3924, doi:10.3748/wjg.v13.i29.3918.
- EMA Defitelio (Defibrotide): Do Not Use for Prophylaxis of Veno-Occlusive Disease (VOD) after Post-Hematopoietic Stem-Cell Transplantation (HSCT) Available online: <https://www.ema.europa.eu/en/medicines/dhpc/defitelio-defibrotide-do-not-use-prophylaxis-veno-occlusive-disease-vod-after-post-hematopoietic> (accessed on 30 August 2022).