from FACS-purified bone marrow mast cells did not find the D816V variant, but rather the M541L polymorphism in the *KIT* gene. Based on this finding, treatment with imatinib 100 mg per day was initiated combined with the ongoing treatment with cromoglycate 200 mg twice a day and ketotifen 1 mg twice a day, with addition of oral antihistamines and steroids during mast cell flares.

During the 4 years of follow-up, the response to treatment has been satisfactory, with good tolerance of imatinib, an attenuation of infiltration in the cutaneous lesions (Fig. 2B) and improvement in systemic symptoms. Occasional episodes of dizziness have resolved with oral dexchlorpheniramine maleate. The patient's growth has been normal, no adverse events have been detected, and laboratory test results and tryptase levels have remained normal.

Activating mutations of the KIT receptor tyrosine kinase have been reported in different types of cancer and in diffuse cutaneous mastocytosis. Imatinib is an oral TKI approved for treatment of systemic mastocytosis in patients with *KIT* mutations outside exon 17, but is generally not effective for D816V-associated disease.[2] The M541L polymorphism found in our patient has been associated with paediatric mastocytosis and a greater sensitivity to imatinib therapy.[3]

The adverse events associated with the use of imatinib include nausea, vomiting, diarrhoea, transaminase elevation, cardiomyopathy, anaemia, thrombocytopenia, granulocytopenia, oedema, skin rash and decreased growth velocity in children.[4,5]

Although there is limited experience in the use of imatinib in children with mastocytosis, it could be an alternative option for patients with DCM and severe symptoms refractory to conventional therapies.

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Transfusion practices of blood products in preterm infants: National survey

Prácticas transfusionales de hemoderivados en recién nacidos prematuros: encuesta nacional

Dear Editor,

It is estimated that 90% of preterm newborns (PTIs) with birth weights of less than 1000 g receive at least one packed red blood cell (PRBC) transfusion and a smaller percentage platelets and/or fresh frozen plasma (FFP) transfusions. However, there is an obvious lack of scientific evidence in relation to the indications and benefits of transfusion practices in this subset of patients.

The recent Effects of Transfusion Thresholds on Neurocognitive Outcomes of Extremely Low-Birth-Weight Infants (ETTNO)[1] and Transfusion of Prematures (TOP)[2] trials have demonstrated that the use of restrictive strategies in the PRBC transfusion is not inferior in terms of survival and neurocognitive outcomes to liberal strategies based on higher haemoglobin thresholds. With regard to platelets, the Platelets for Neonatal Thrombocytopenia (PlaNeT-2)/Management of Thrombocytopenia in Special Subgroup (MATISSE)[3] trial compared a liberal (50 000/dL) threshold for the indication of transfusion with a more restrictive one (25 000/dL), and found higher rates of death and major bleeding in the high-threshold group. These studies evinced the lack of knowledge of the pathophysiological processes underlying haematological disorders in PTIs.

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Table 1 Data of the national survey of transfusion protocols.

Thresholds for transfusion of packed red blood cells in different clinical scenarios, median (IQR), expressed in g/dL			
	<1 week	1–2 weeks	>2 weeks
No O_2	10 (10)	9.5 (8–10)	8 (7–8.5)
Low-flow O_2	10 (10–11)	10 (9–10)	8.5 (8–9)
O_2 with FiO_2 < 30	12 (11–12)	10 (10–12)	9.5 (8–10)
O_2 with FiO_2 > 30	12 (12–12)	11 (10–12)	10 (9.5–10)
Mechanical ventilation	12 (12)	12 (10–12)	10 (10–11)
Volume: 15 mL/kg (IQR, 15–20 mL/kg)			
Transfusion time: 3 h (IQR, 2–4 h)			

Thresholds for platelet transfusion in different clinical scenarios (median, (IQR) expressed in platelets/dL)		
	<28 weeks	28–32 weeks
No bleeding	30 000 (20–50 × 10^3)	25 000 (25–30 × 10^3)
Bleeding	50 000 (50–100 × 10^3)	50 000 (50–90 × 10^3)
Volume: 15 mL/kg (IQR, 10–15 mL/kg)		
Transfusion time: 2 h (IQR, 2–3 h)		

Indications for transfusion of fresh frozen plasma	
Coagulopathy with bleeding	100%
Coagulopathy without bleeding	43.9%
Bleeding without coagulopathy	39%
Hypotension	4.9%
Volume: 15 mL/kg (IQR, 12.5–15 mL/kg)	
Duration of transfusion: 3 h (IQR, 3–4 h)	

The table presents the thresholds for packed red blood cells and platelet transfusion, expressed as median and interquartile range (IQR), for different clinical scenarios and gestational ages. It also includes information on the median volume administered and the median duration of transfusion, as well as the indications for fresh frozen plasma.

In light of this situation, a European survey was carried out on the initiative of the Neonatal Transfusion Network, with participation of 343 centres in 18 countries.[4] In this framework, we carried out a substudy between December 2020 and April 2021 in level III neonatal units in Spain to assess the customary clinical practice in the use of blood products in PTI born at or before 32 weeks of gestation and analyse how it compares to the results of the most recent clinical trials and with the current overall situation in the Europe.

To do so, we used an online that was sent to the main neonatal intensive care units across Spain. We contacted a total of 58 units, of which 41 (70%) responded. Table 1 presents the results regarding transfusion practices. In general, there was little variability between the surveyed facilities in the haemoglobin threshold used to determine the indication of transfusion support. The median PRBC volume delivered in Spanish hospitals was 15 mL/kg (interquartile range [IQR]: 15–20 mL/kg), the volume of platelets 15 mL/kg (IQR, 10–15 mL/kg) and the volume of FFP 15 mL/kg (IQR, 12.5–15 mL/kg). When it came to the indications for the administration of FFP, there was consensus in regard to its use for management of coagulopathy associated with bleeding. However, there were significant discrepancies between the surveyed centres in regard to other indications, such as coagulopathy without bleeding and bleeding in the absence of coagulopathy.

Fig. 1 compares the applied haemoglobin thresholds to the thresholds established in the trials mentioned above.[1,2] We found that, on average, 13.3% of Spanish units applied restrictive thresholds, 83% intermediate thresholds and 3.5% liberal thresholds. In the European survey, up to 30% of the units applied restrictive thresholds, more than double the percentage in Spain, and 68% applied intermediate thresholds. Recently, the Standards Committee of the Sociedad Española de Neonatología (SENeo) published recommendations to standardise the transfusion of blood products in neonatal care nationwide.[5] Fig. 1 presents the comparison of real-world practice with the thresholds recommended by the SENeo, evincing good concordance with recommendations in the first two weeks of life, but the use of much more liberal thresholds after the second week.

As regards the thresholds applied for the transfusion of platelets, in PTIs delivered before 28 weeks, 37% of

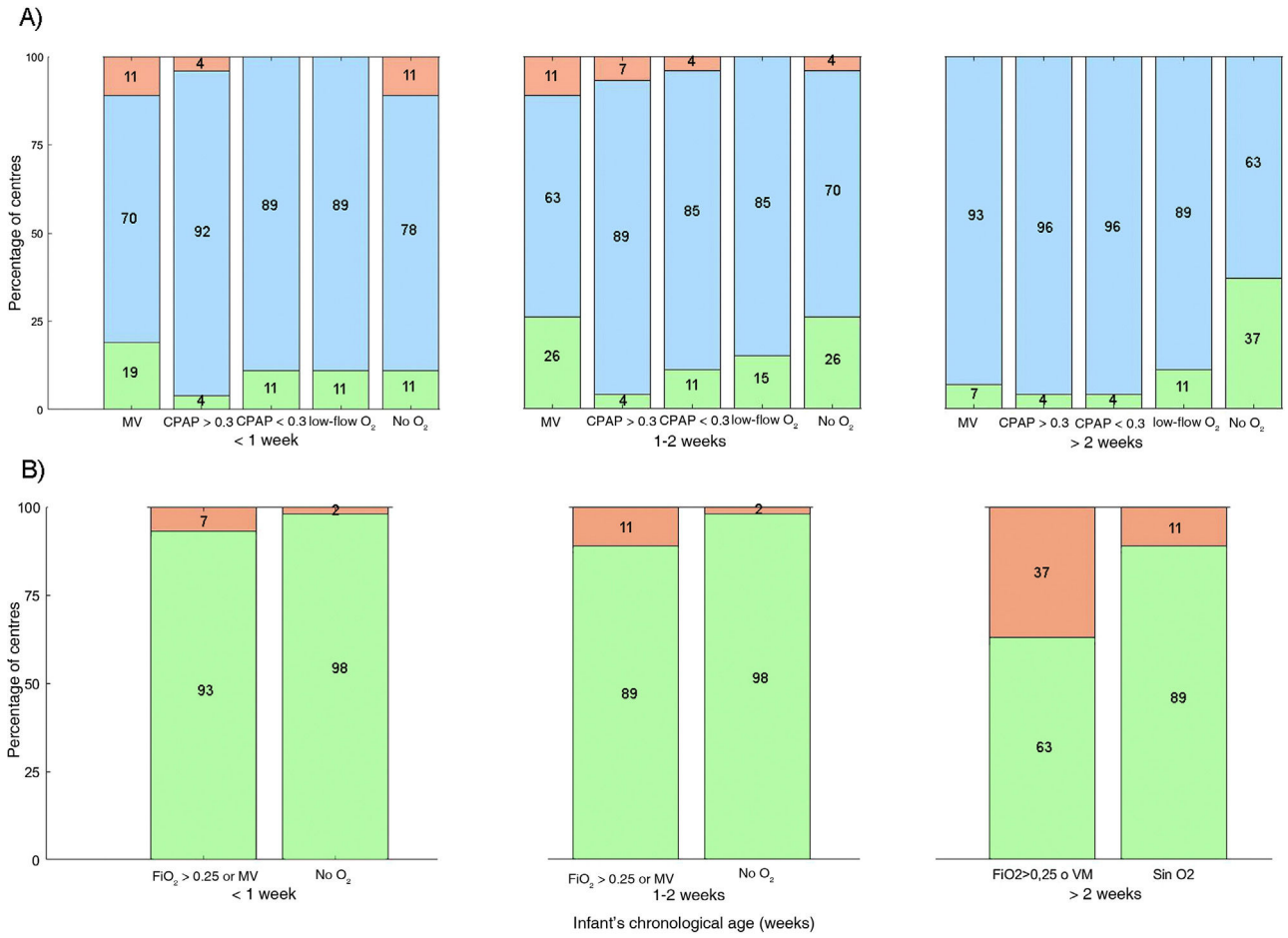

Figure 1 Current situation of PRBC transfusions in relation to the thresholds used in the ETTNO and TOP clinical trials (A) and the recommendations of the SENeo (B). Data presented in stacked bar charts showing the percentage of neonatal units that use different PRBC transfusion thresholds in different clinical scenarios and in infants with different gestational ages (weeks). In the charts at the top, the reference thresholds are those reported for the ETTNO and TOP trials: (A) at or below the restrictive (green), between the restrictive and liberal thresholds (blue) and above the liberal threshold (red). At the bottom, the thresholds correspond to the recommendations of the SENeo (B): at or below the threshold (green) and above the threshold (red). The colours of the figure can only be seen in the online version.

the centres applied a restrictive threshold, a percentage that rose to 57% for PTIs delivered between 28 and 32 weeks. These results were similar to those of the European survey and in agreement with the recommendations derived from the findings of the PlaNeT2/MATISSE trial.

Based on our findings, we ought to highlight that Spanish neonatal units have more restrictive policies when it comes to platelet transfusion compared to the thresholds applied for the treatment of anaemia, which suggests an uneven application of scientific evidence to clinical practice. The most liberal transfusion policies beyond the first two weeks of life suggest a tendency to maintain the same transfusion thresholds established in the first weeks. In addition, there was substantial variability in the indications for FFP.

In conclusion, our study evinced that transfusion policies diverged from recommendations in varying degrees. The fact that a large majority of hospitals used local protocols may be one of the factors contributing to the observed heterogeneity and hindering the application of the most recent evidence. These findings underscore the need to continue to promote research on transfusion, which will contribute to increase the quality and safety of the care provided to PTIs.

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Familial lymphohistiocytosis, the importance of recognizing the infrequent

Linfohistiocitosis familiar, la importancia de reconocer lo infrecuente

Dear Editor:

A boy aged 2 years presented with fever of 6 days' duration (40 °C) in October 2020, without symptoms of upper respiratory tract infection or vomiting. The urine was dark and the stools were normal. The patient had not been exposed to SARS-CoV-2, there were no animals in the household and he had no history of recent travel (the family was from Pakistan and had been in Spain since March 2020). He was the single child of a healthy consanguineous couple, with no other history of interest. There had been no complications during pregnancy, delivery or the perinatal period. The patient was correctly vaccinated according to the Pakistani vaccination schedule, and this was his first episode of febrile illness.

The paediatric assessment triangle indicated the patient was stable. His temperature was 39.7 °C. Other symptoms included pallor, mucosal dryness, conjunctival icterus, a murmur grade I/VI at the level of the mesocardium, normal pulses, painless hepatomegaly and palpable spleen tip. There was a small amount of tonsillar exudate and mild cervical lymph node enlargement.

In addition to the SARS-CoV-2 antibody test, a complete blood count with differential and blood chemistry panel were ordered, of which the salient findings were microcytic hypochromic anaemia (red blood cells, 8 g/dL), mild neutropaenia with a normal white blood cell count and thrombopenia (75 000 platelets/mm^3) without morphological abnormalities. The Coombs test was negative. The bilirubin level was 10 mg/dL, with elevation of alanine aminotransferase (ALT, 413 IU/L; normal range: 1–55) and lactate dehydrogenase (LDH, 1176 IU/L; normal: 125–243) and decreased sodium (Na, 128 mEq/L; normal: 136–145). The urinalysis was normal. The evaluation also included an Epstein-Barr virus (EBV)/cytomegalovirus (CMV) test; testing for leishmaniasis (endemic country of origin) and a thick blood film examination. The Mantoux test reaction measured 0 mm and imaging tests evinced hepatosplenomegaly in the absence of other abnormalities.

After performing the initial tests and given the presentation with decreased appetite, hepatosplenomegaly, cytopenia and hypoalbuminaemia in a patient from a region with a high burden of leishmaniasis, treatment was initiated with liposomal amphotericin B. The bone marrow (BM) examination was normal, with no evidence of haemophagocytosis or morphology suggestive of leishmaniasis. The EBV polymerase chain reaction (PCR) test turned out positive, while serological tests for detection of *Leishmania* were negative, leading to diagnosis of primary infection by EBV. The patient became afebrile within 24 h and, having ruled out leishmaniasis, treatment with amphotericin B was discontinued. At the haematological level, there were signs of BM regeneration and stabilization of haemoglobin levels from 48 h, and the patient did not require transfusion.

In addition to the cytopenias and liver involvement, the evaluation evinced Hyperferritinaemia (ferritin, 7251 ng/mL; normal: 15–120) and increased levels of the soluble interleukin (IL)-2 receptor (>7500 IU/L).

On account of the hepatic involvement and hypertriglyceridemia, lysosomal acid lipase deficiency was ruled out, and apolipoprotein test results were normal.

The presence of fever associated with cytopenias, elevation of ferritin, LDH and soluble IL-2 receptor, hypofibrinogenaemia combined with hypertriglyceridemia, hypertransaminasaemia and hyperbilirubinaemia, despite a normal BM, suggested the diagnosis of haemophagocytic syndrome secondary to acute infection by EBV.

Given the age of the patient, the rarity of the presentation and the consanguinity of the parents, genetic testing was performed for screening of primary haemophagocytic syndromes, confirming the presence of

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