

Transfusiones y uso de EPO en RNPT.

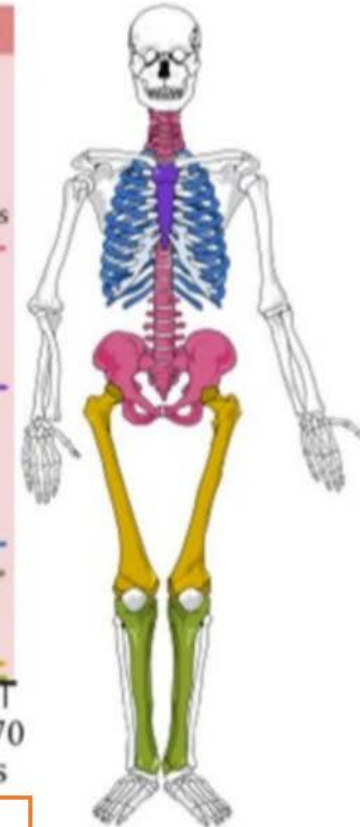
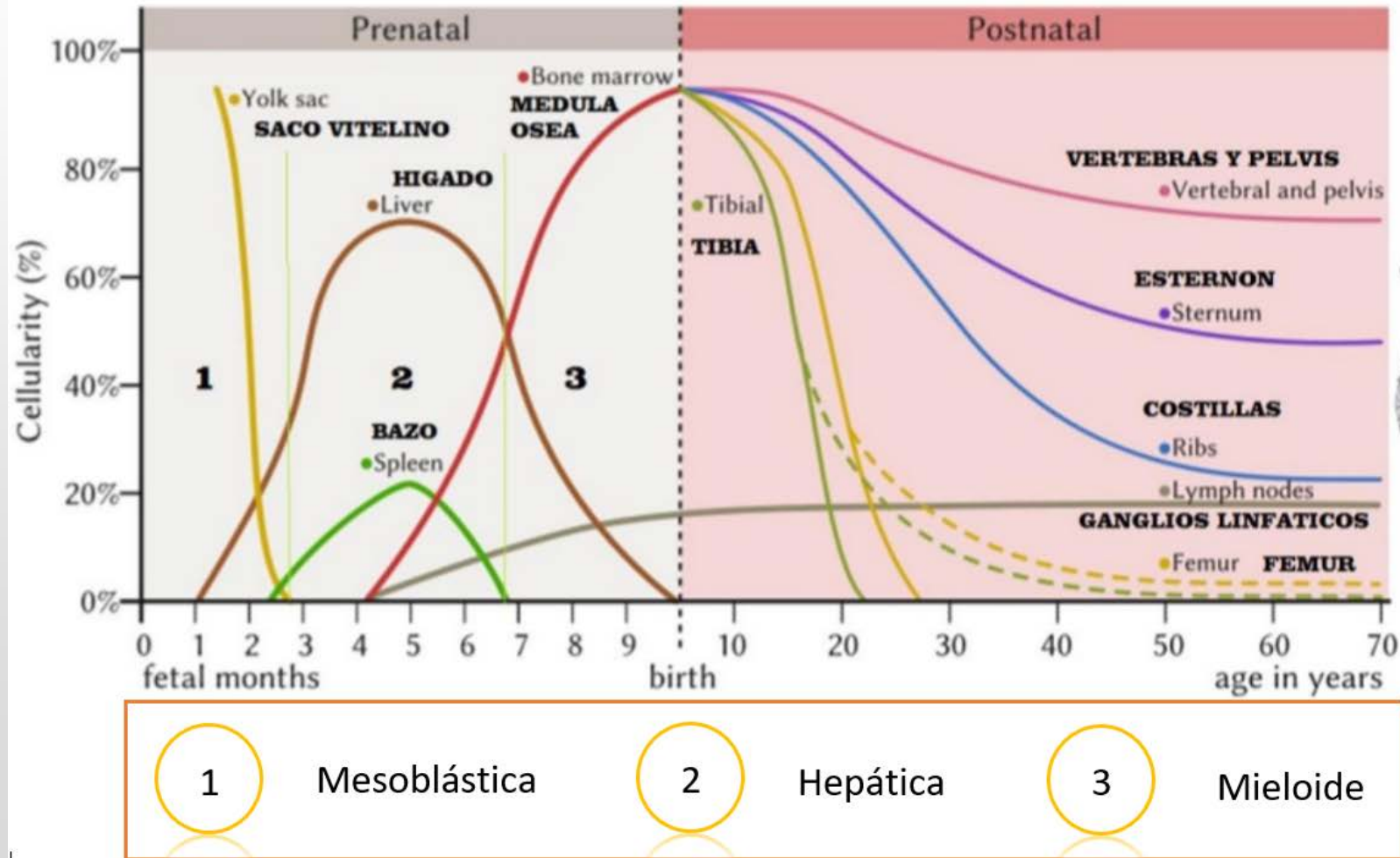
INTERNA: KRYSTEL VOLGGER.

DOCENTE: DR. GERARDO FLORES.

INTERNADO PEDIATRÍA –
ROTACIÓN NEONATOLOGÍA.

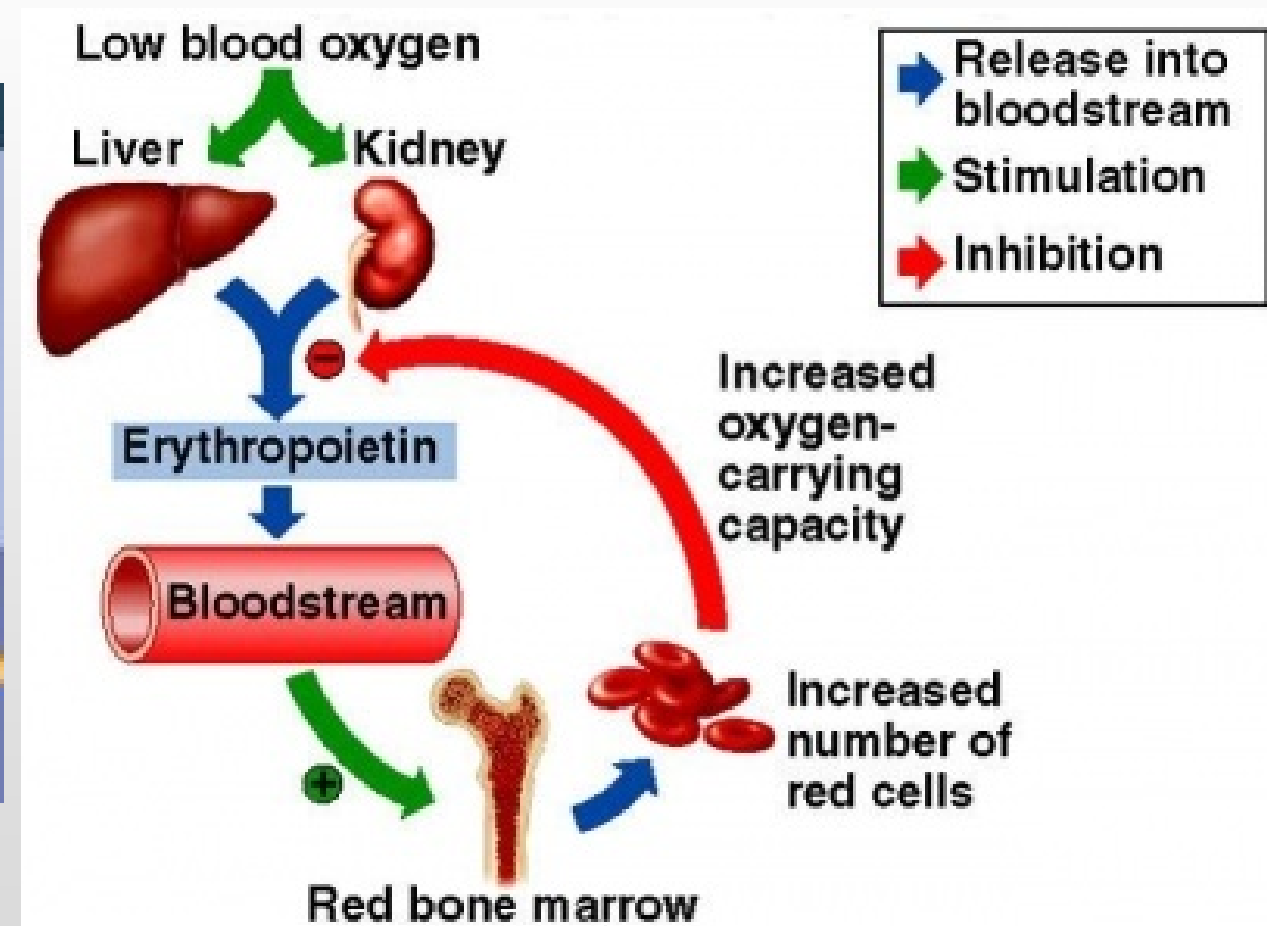
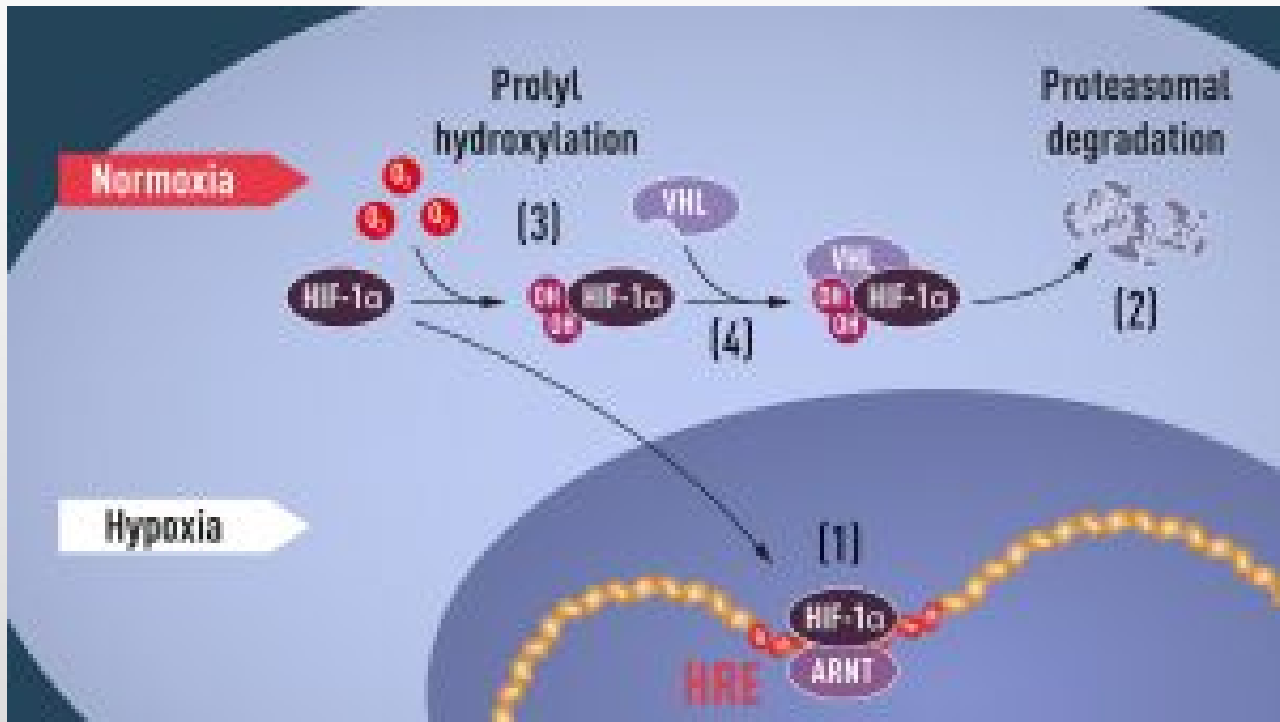


Hematopoyesis intrauterina y primeros momentos de vida.



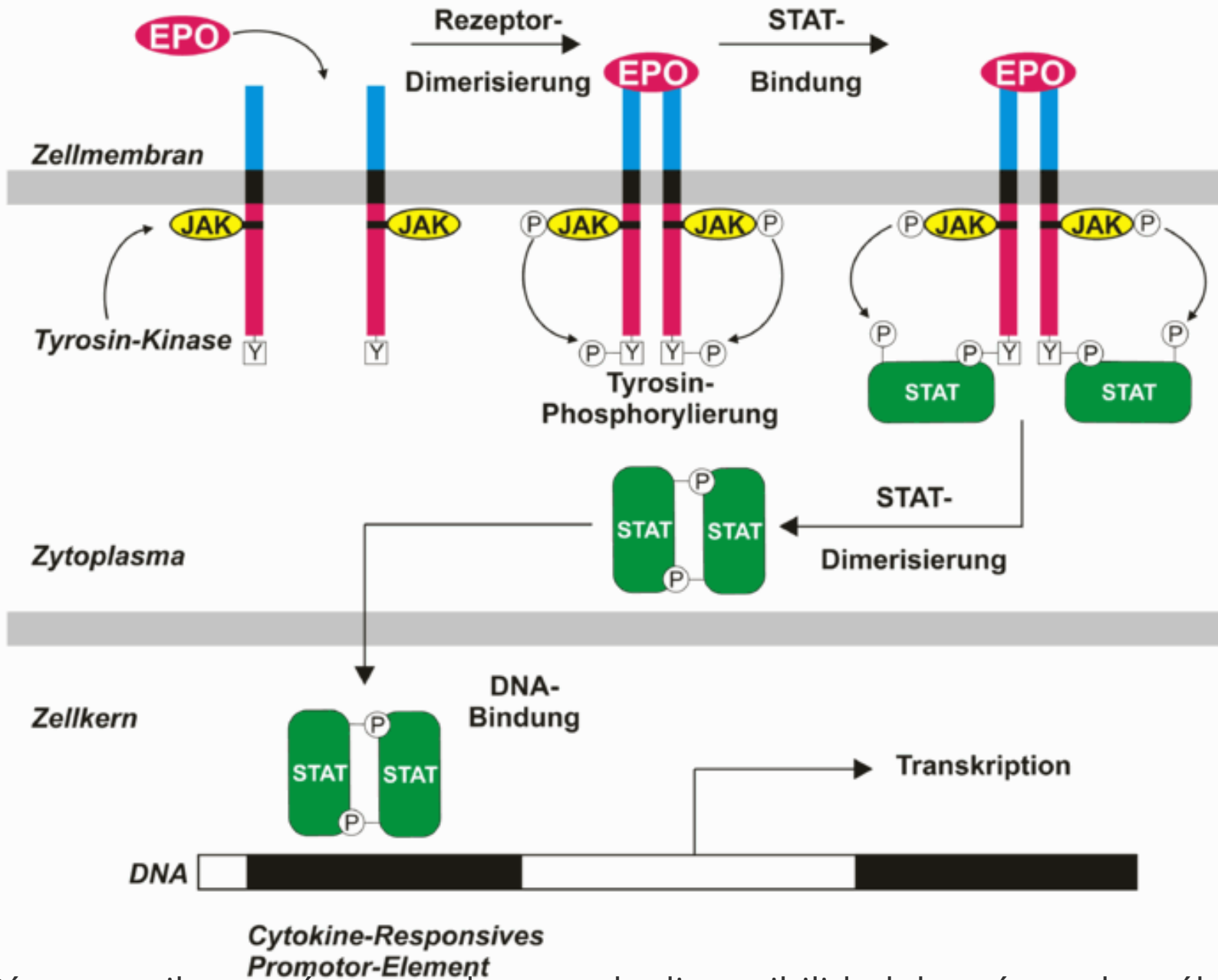
Hematopoyesis: claves de la generación de todas las células sanguíneas. Inmunología celular y molecular, de Abbas, Lichtman & Pillai. 9ª Edición (2019).

Eritropoyesis - Molecular



Cómo perciben y cómo se adaptan a la disponibilidad de oxígeno las células de nuestro cuerpo. Kaelin, Semenza, Ratcliffe (2019) Ganadores del Premio Nobel de Fisiología 2019.

Efectos de EPO.



Cómo perciben y cómo se adaptan a la disponibilidad de oxígeno las células de nuestro cuerpo. Kaelin, Semenza, Ratcliffe (2019) Ganadores del Premio Nobel de Fisiología 2019.

Efectos de EPO.

Regula tiempos de ciclo celular.

Acorta tiempo división y maduración.

Favorece salida GR inmaduros.

Estimula liberación de reticulocitos.

Aumenta velocidad síntesis de Hb (transferrina).

Características del Eritrocito Neonatal:

VM 60 - 70 días RNT // 35 - 50 días RNPT.

Mayor VCM y menor HCM.

Frotis → dismorfia alta, mayor en RNPT.

HbF → HbA primeras semanas.

Tasa de síntesis Hb y GR disminuye primeros días.

Anemia Neonatal.

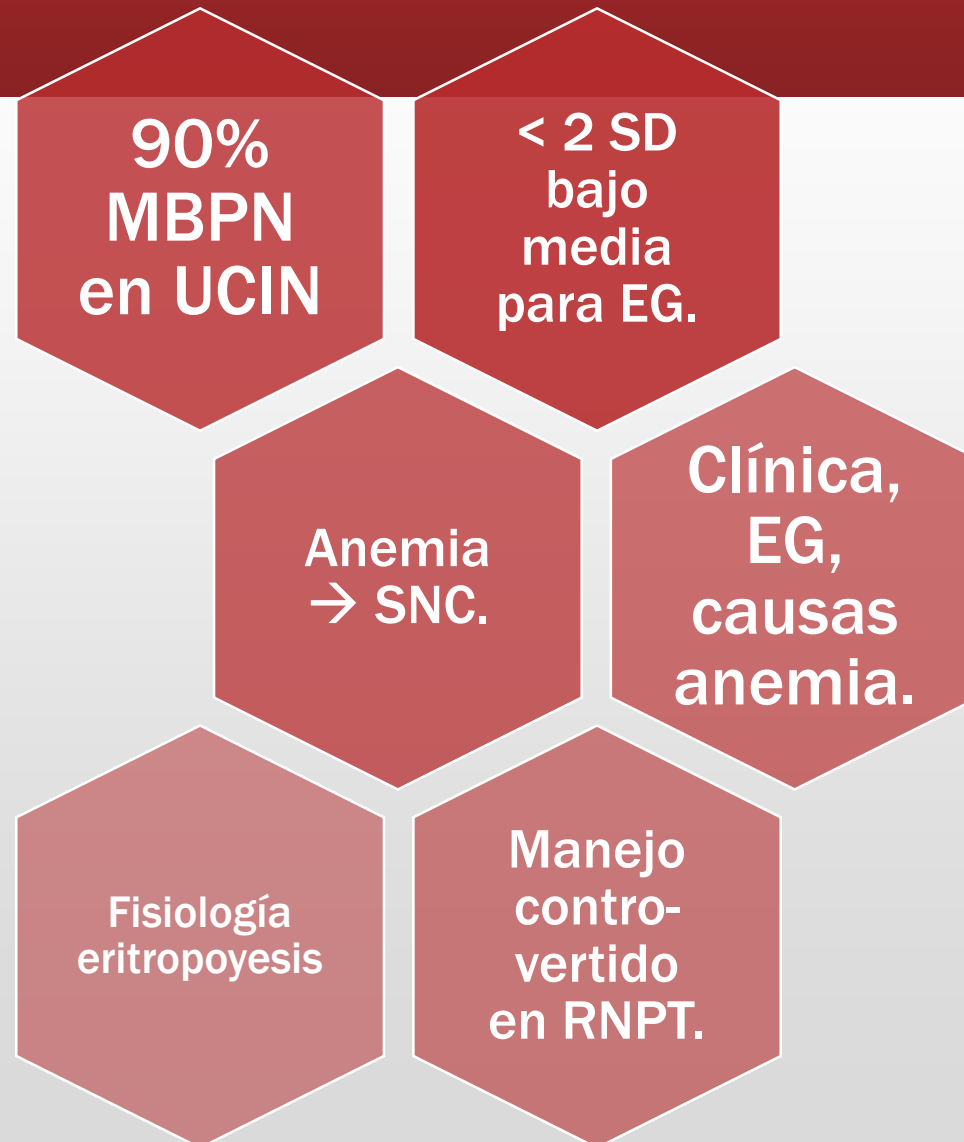


Table 1

Reference hematologic values in term newborns (adapted from Italian National Guidelines) [23].

Age	Hb (g/dL)		Hct (%)		RBC ($10^{12}/L$)		MCV (fL)		MCH (pg)	
	Mean	-2 SD	Mean	-2 SD	Mean	-2 SD	Mean	-2 SD	Mean	-2 SD
Cord blood	16.5	13.5	51	42	4.7	3.9	108	98	34	31
1-3 days	18.5	14.5	56	45	5.3	4.0	108	95	34	31
7 days	17.5	13.5	54	42	5.1	3.9	107	88	34	28
14 days	16.5	12.5	51	39	4.9	3.6	105	86	34	28
4 weeks	14.0	10.0	43	31	4.2	3.0	104	85	34	28
8 weeks	11.5	9.0	35	28	3.8	2.7	96	77	30	26
12 weeks	11.5	9.0	35	29	3.8	3.1	91	74	30	25

Hb, hemoglobin; Hct, hematocrit; RBC, red blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin.

Table 2

Reference hemoglobin (Hb) values in preterm newborns (adapted from Italian National Guidelines) [23].

Age (weeks)	Hb according to birth weight	
	1000–1500 g	1501–2000 g
2	16.3 (11.7–18.4)	16.8 (11.8–19.6)
4	10.9 (8.7–15.2)	11.5 (8.2–15)
8	8.8 (7.1–11.5)	9.4 (8.0–11.4)
12	9.8 (8.9–11.2)	10.2 (9.3–11.8)
16	11.3 (9.1–13.1)	11.3 (9.1–13.1)

Causas de Anemia:



Anemia fisiológica de la infancia.

Primera respiración → aumenta disponibilidad de O₂ → down regulation EPO.

Cambio HbF por HbA → cambio afinidad O₂.

EPO cae hasta 6 - 12 semanas → nadir de HTO/Hb.

Nadir → HTO cercano a 30% y Hb 10 - 12 g/dL.

Anemia de Prematuridad:

Exageración de anemia fisiológica → RNPT < 32 SDG → reticulocitos bajos, EPO baja.

A menor edad nadir más bajo y precoz.

Bajo nivel de EPO → producción disminuida y acelerado catabolismo.

No acelera transición hígado a riñón → 20% menos de precursores.

Enfrentamiento diagnóstico:



Tratamiento de la Anemia.



VS



Riesgos de transfusión.

Sobrecarga Volumen	Hiperkalemia	NEC	Rx febril no hemolítica
Hemolisis no inmune	Enfermedad injerto contra huésped	TRALI	Contaminación bacteriana
Sensibilización a antígenos eritrocitarios	Infecciones virales.	Rx alérgicas	Rx hemolítica tardía.

G. Arcam; X. Cabonell-Estrany. (2008). Anemia Neonatal. Protocolos Terapeuticos de la AEP: Neonatología. 362-371.

Protocolo de indicación transfusional en paciente neonatal. HPM (2019 - 2024).

Table 3. Primary and Secondary End Points

End points	Liberal transfusion threshold	Restrictive transfusion threshold	Absolute difference, % (95% CI) ^a	Odds ratio or adjusted difference in least-square means (95% CI) ^b	P value ^c
Primary end point					
Death or neurodevelopmental impairment by 24 mo, No./total (%) ^d	200/450 (44.4)	205/478 (42.9)	1.6 (-4.8 to 7.9)	1.05 (0.80 to 1.39)	.72
Secondary end points					
Death by 24 mo, No./total (%)	38/460 (8.3)	44/491 (9.0)	-0.7 (-4.3 to 2.9)	0.91 (0.58 to 1.45) ^e	.70
Cognitive deficit, No./total (%) ^f	154/410 (37.6)	148/430 (34.4)	3.1 (-3.3 to 9.6)	1.12 (0.83 to 1.51)	.47
Cognitive deficit defined by Bayley 2 MDI score, No./total (%) ^f					
<85	143/378 (37.8)	139/387 (35.9)	1.9 (-4.9 to 8.8)	1.09 (0.81 to 1.46) ^e	.58
<70	71/378 (18.8)	62/387 (16.0)	2.8 (-2.6 to 8.1)	1.21 (0.83 to 1.76) ^e	.31
Bayley 2 MDI score, mean (SD) ^f	92.6 (16.5) [n = 336]	92.4 (17.5) [n = 360]	0.2 (-2.4 to 2.7)	0.4 (-2.1 to 2.9) ^g	.75
Cerebral palsy, No./total (%)	18/419 (4.3)	25/443 (5.6)	-1.3 (-4.2 to 1.5)	0.75 (0.40 to 1.40) ^e	.37
Bayley 2 PDI score, mean (SD) ^f	89.3 (15.1) [n = 315]	89.2 (15.4) [n = 312]	0.0 (-2.4 to 2.4)	0.1 (-2.0 to 2.2) ^g	.92
GMFCS score I-V, No./total (%) ^h	34/416 (8.2)	42/440 (9.5)	-1.4 (-5.2 to 2.4)	0.84 (0.53 to 1.36) ^e	.48
Severe visual impairment, No./total (%) ⁱ	10/417 (2.4)	12/443 (2.7)	-0.3 (-2.4 to 1.8)	0.88 (0.61 to 2.07) ^e	.77
Severe hearing impairment, No./total (%) ^j	4/418 (1.0)	6/443 (1.4)	-0.4 (-1.8 to 1.0)	0.70 (0.20 to 2.51) ^e	.59
Length of hospital stay, mean (SD), d	93 (41) [n = 489]	92 (38) [n = 510]	0.7 (-4.2 to 5.6)	-0.0 (-4.7 to 4.7) ^g	1.00
Duration of support, postnatal age, mean (SD), d ^k					
At end of invasive ventilatory support ^l	23 (28) [n = 298]	23 (26) [n = 321]	0.1 (-4.2 to 4.3)	0.0 (-4.1 to 4.1) ^g	1.00
At last positive pressure respiratory support ^l	53 (31) [n = 451]	53 (29) [n = 475]	0.5 (-3.3 to 4.6)	-0.1 (-3.4 to 3.1) ^g	.94
At last supplemental oxygen	52 (33) [n = 371]	50 (33) [n = 378]	2.7 (-2.1 to 7.4)	1.6 (-2.5 to 5.8) ^g	.44
At last caffeine administration	69 (26) [n = 417]	70 (26) [n = 425]	-1.0 (-4.6 to 2.5)	-2.0 (-5.1 to 1.1) ^g	.20
At end of gavage feeding	75 (25) [n = 422]	77 (27) [n = 441]	-1.6 (-5.1 to 1.8)	-2.6 (-5.5 to 0.4) ^g	.09

Transfusión liberal vs restrictiva.

Axel, F. (11/08/2020). ETTNO. JAMA, 324 (6), 560 - 570. 10/09/2020

Carson JL. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database of Systematic Reviews 2016, Issue 10. Art.

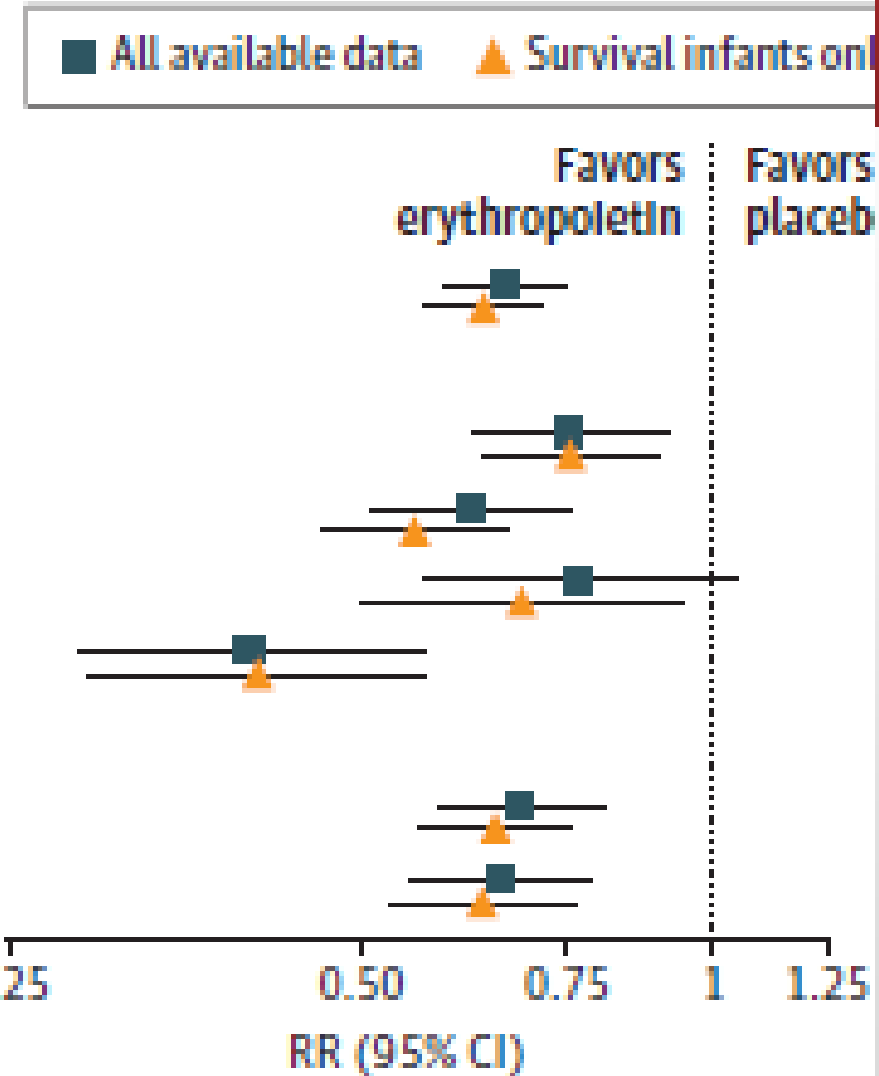
Effect of High-dose EPO on blood Tx in extremely low gestational age neonates.



Resultados:

A No. of pRBC transfusions

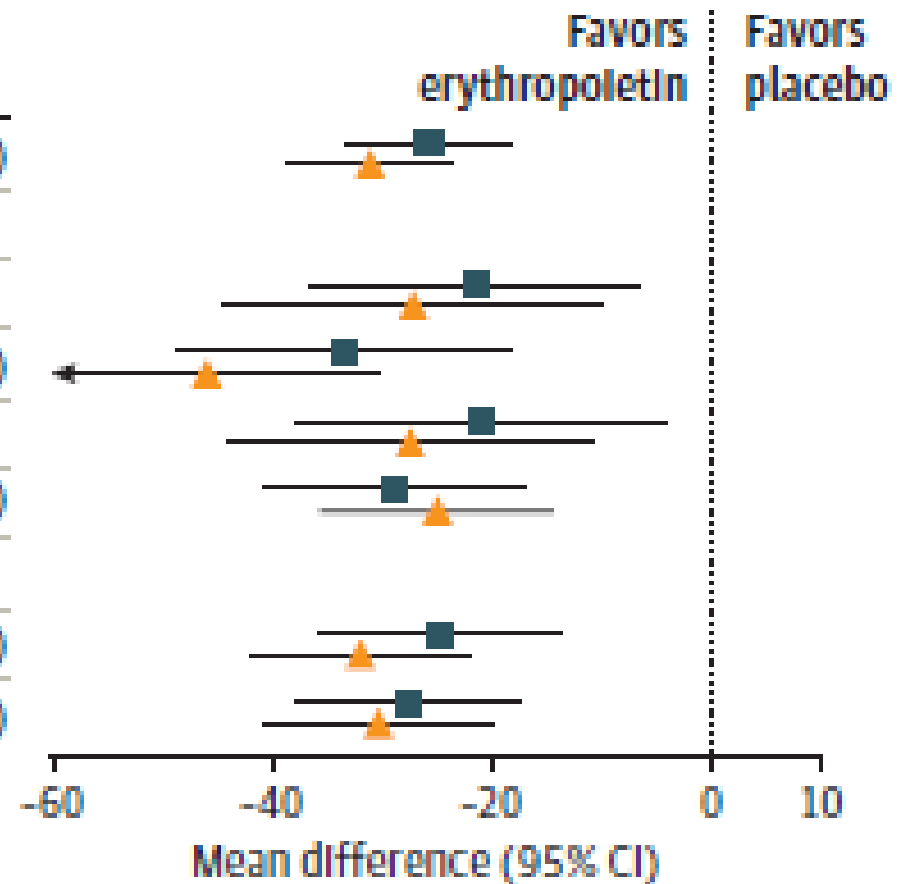
Source	Mean (SD) No. of transfusions		RR (95% CI)
	Erythropoietin group	Placebo group	
Overall	3.5 (4.0)	5.2 (4.4)	0.66 (0.59-0.75)
By gestational age at birth, wk			
24 (n = 232)	6.4 (4.5)	7.8 (4.8)	0.75 (0.62-0.91)
25 (n = 245)	3.8 (2.8)	6.0 (4.2)	0.62 (0.51-0.75)
26 (n = 221)	3.0 (4.5)	3.6 (3.4)	0.77 (0.57-1.04)
27 (n = 238)	1.1 (1.8)	3.0 (3.1)	0.40 (0.29-0.56)
By sex			
Female (n = 448)	3.2 (3.8)	5.0 (4.3)	0.66 (0.55-0.78)
Male (n = 488)	3.7 (4.1)	5.5 (4.5)	0.68 (0.58-0.80)



Resultados.

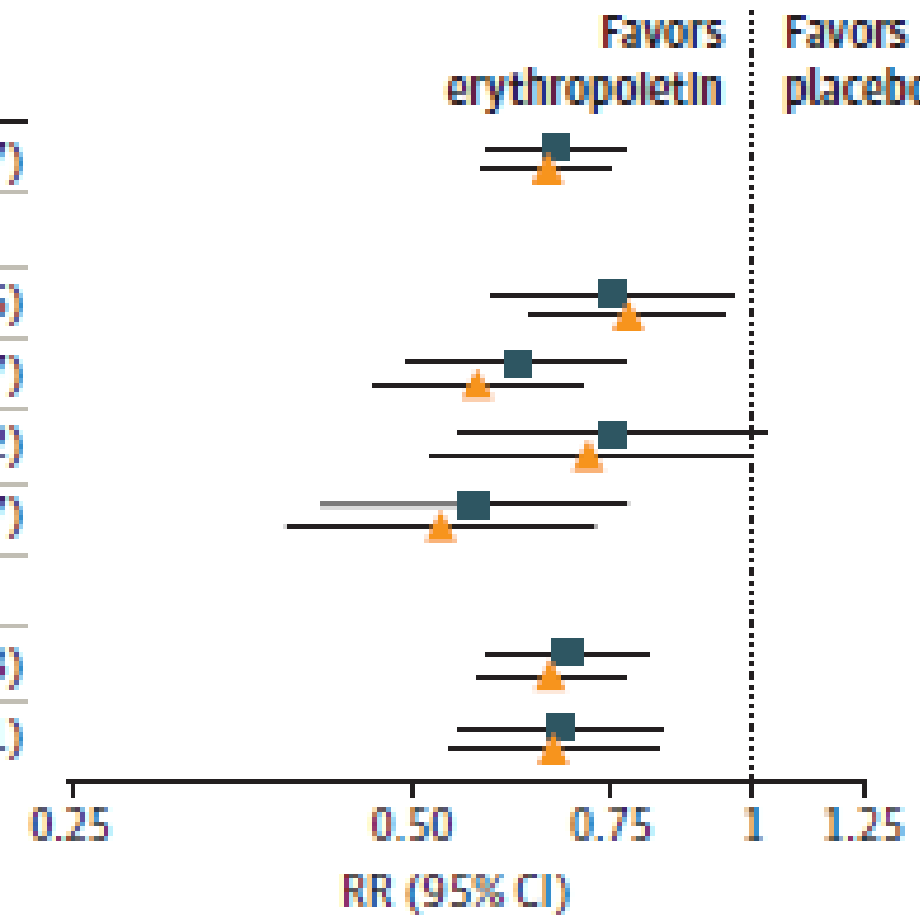
B Cumulative volume of pRBC transfusions

Source	Mean (SD) No. of transfusions		Mean difference (95% CI)
	Erythropoietin group	Placebo group	
Overall (n = 936)	47.6 (60.4)	76.3 (68.2)	-25.66 (-33.26 to -18.07)
By gestational age at birth, wk			
24 (n = 232)	77.5 (66.1)	99.7 (67.0)	-21.42 (-36.45 to -6.38)
25 (n = 245)	52.5 (49.6)	87.3 (70.5)	-33.32 (-48.47 to -18.17)
26 (n = 221)	44.6 (72.8)	62.2 (69.2)	-20.97 (-37.77 to -4.18)
27 (n = 238)	21.2 (38.8)	51.5 (52.6)	-28.73 (-40.45 to -17.00)
By sex			
Female (n = 448)	38.7 (51.9)	69.8 (65.9)	-27.53 (-37.56 to -17.50)
Male (n = 488)	55.2 (66.0)	82.8 (70.0)	-24.53 (-35.55 to -13.51)



Resultados

Source	Mean (SD) donor exposure		RR (95% CI)
	Erythropoietin group	Placebo group	
Overall (n = 936)	1.6 (1.7)	2.4 (2.0)	0.67 (0.58-0.77)
By gestational age at birth, wk			
24 (n = 232)	2.5 (1.8)	3.0 (2.3)	0.75 (0.59-0.96)
25 (n = 245)	1.7 (1.3)	2.8 (2.1)	0.62 (0.50-0.77)
26 (n = 221)	1.4 (2.0)	1.8 (1.5)	0.75 (0.55-1.02)
27 (n = 238)	0.8 (1.2)	1.6 (1.5)	0.57 (0.41-0.77)
By sex			
Female (n = 448)	1.5 (1.9)	2.2 (2.0)	0.67 (0.55-0.83)
Male (n = 488)	1.6 (1.5)	2.5 (2.0)	0.69 (0.58-0.81)

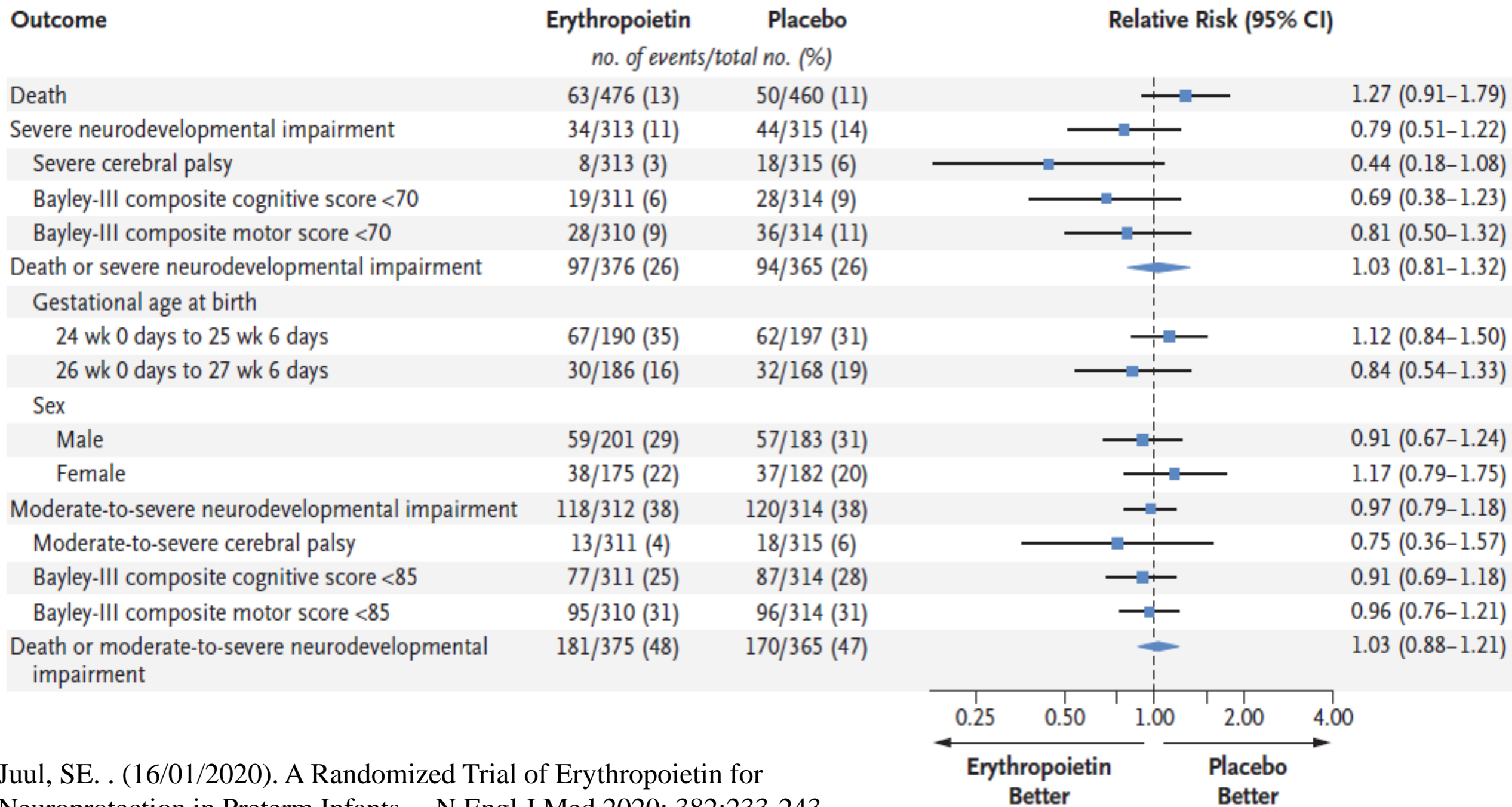


A randomized trial of EPO for neuroprotection in RNPT.

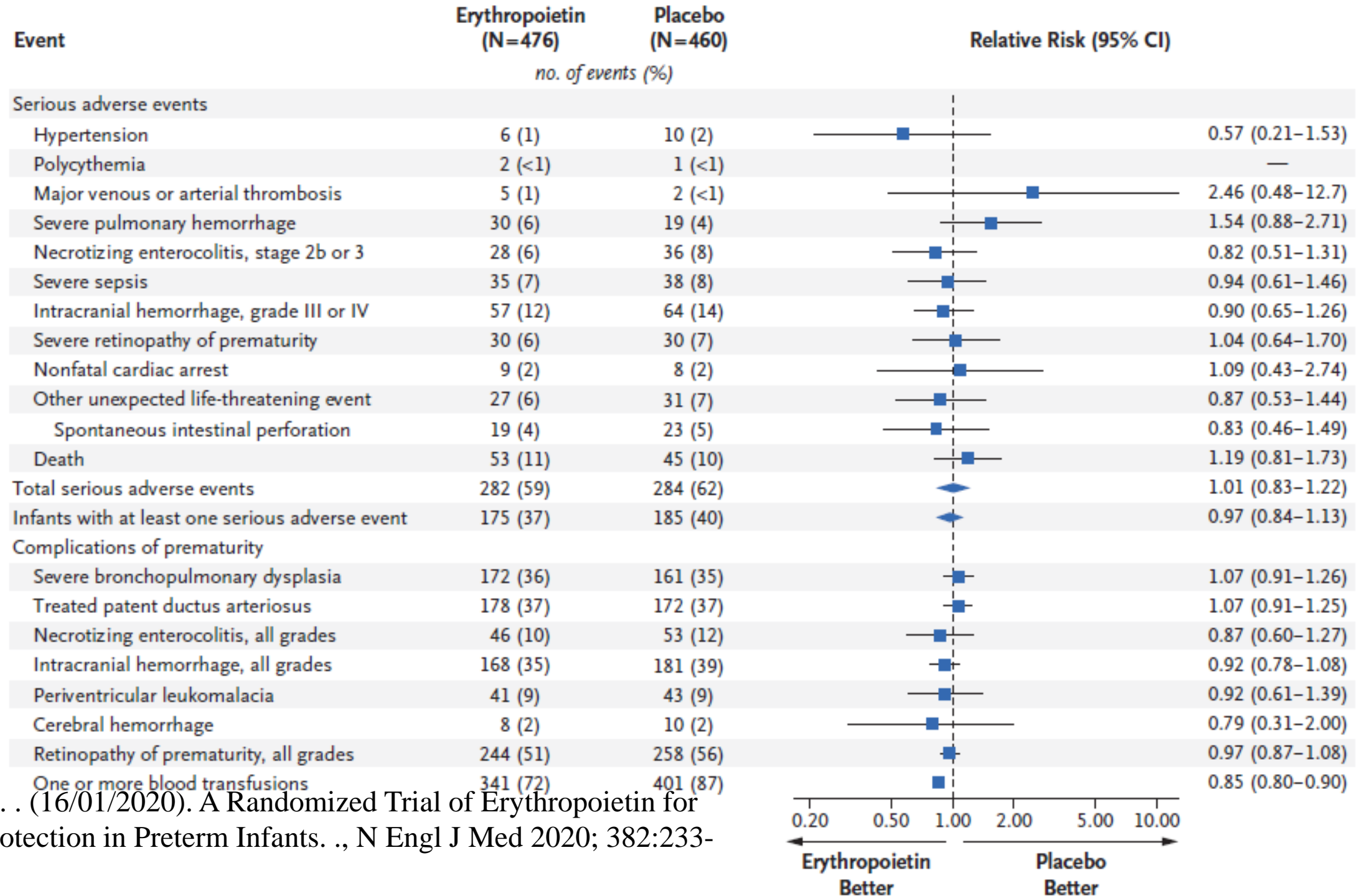
EPO vs placebo → mortalidad y desarrollo neuronal a 2 años.

Retinopatía del prematuro, hemorragia intracraneal, sepsis, NEC, displasia broncopulmonar, parálisis cerebral.

Efectos adversos.



Juul, SE. . (16/01/2020). A Randomized Trial of Erythropoietin for Neuroprotection in Preterm Infants. ., N Engl J Med 2020; 382:233-243, ..



Juul, SE. . (16/01/2020). A Randomized Trial of Erythropoietin for Neuroprotection in Preterm Infants. ., N Engl J Med 2020; 382:233-243, ..

Perinatal iron deficiency: implications for mothers and infants.

30% MEF.
38%
embarazadas.

Uso en cerebro,
corazón y
músculo.

Redistribución
del Fe corporal.

Déficit cognitivo
y
comportamiento
anómalo.

Implicaciones en
la madre.

Conclusiones.

Disminuye n°
de tx.

Disminuye
volumen Tx.

Disminuye
exposición.

Neuroprotección
y mortalidad.

Efectos
adversos

Bibliografía:

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- **Cómo perciben y cómo se adaptan a la disponibilidad de oxígeno las células de nuestro cuerpo.** Kaelin, Semenza , Ratcliffe (2019) Ganadores del Premio Nobel de Fisiología 2019.
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- **Protocolo de indicación transfusional en paciente neonatal.** HPM (2019 – 2024).
- Juul, S. E., Derman, R. J., & Auerbach, M. (2019). Perinatal iron deficiency: implications for mothers and infants. *Neonatology*, 115(3), 269-274.

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