TABELLA 3. INDICAZIONI OFF LABEL A BASSA PRIORITÀ
DA VALUTARE NEI SINGOLI CASI, DOPO FALLIMENTO DEI TRATTAMENTI APPROVATI O IN CASO DI CONTROINDICAZIONE ALL'IMPIEGO DEGLI STESSI

CONDIZIONE	TERAPIA DI RIFERIMENTO	SCHEMA IVIG	NOTE
		IMMUNOLOGIA	
Sindrome da immunità anti-fosfolipidica (sindrome catastrofica, perdite fetali ricorrenti) Prevenzione secondaria delle complicanze della gravidanza per i pazienti con sindrome ostetrica da anticorpi antifosfolipidi (APS) e storia di natimortalità	TPE, anticoagulanti. In studio eculizumab, inibitore del complemento attivato.	In aggiunta ad anticoagulanti e TPE. IVIg 0.4-0.5g/kg per 2-5 gg/mese per 3 mesi, poi rivalutazione.	Rodriguez-Pintó I, Espinosa G, Group CRP. The effect of triple therapy on the mortality of catastrophic anti-phospholipid syndrome patients. Rheumatology (Oxford) 2018; 57: 1264–70. Rodriguez-Pintó I, Lozano M, et al. Plasmaexchange in catastrophic antiphospholipidsyndrome. Presse Med 2019;48:347–53. Tenti S, Cheleschi S, et al Intravenous immunoglobulins and antiphospholipid syndrome: How, when and why? A review of the literature. Autoimmun Rev 2016; 15: 226–35. Marinho A, Delgado Alves J, Fortuna J, et al. Biological therapy in systemic lupus erythematosus, antiphospholipid syndrome, and Sjögren's syndrome: evidence- and practice-based guidance. Front. Immunol 2023; 14:1117699 Urban ML, Bettiol A, Serena C, et al. Intravenous immunoglobulin for the secondary prevention of stillbirth in obstetric antiphospholipid syndrome: A case series and systematic review of literature. Autoimmun Rev 2020;19(9):102620.
		EMATOLOGIA	
Aplasia dei globuli rossi acquisita, associata o meno a infezione da parvovirus B19	PDN, immunosoppressori	Terapia immunomodulante: IVIg 0.4-0.5g/kg per 2-5 gg/mese	Crabol Y, Terrier B, et al. Intravenous immunoglobulin therapy for pure red cell aplasia related to human parvovirus b19 infection: a retrospective study of 10 patients and review of the literature. Clin Infect Dis. 2013;56(7):968-77. Balasubramanian SK, Sadaps M, et al. Rational management approach to pure red cell aplasia. Haematologica 2018;103(2):221-30. Bian Z, Zhou N, et al. Evaluating the Efficacy and Anti-infective Effect of High-dose Intravenous Immunoglobulin Adjuvant Therapy for Acquired Aplastic Anemia Children. J Pediatr Hematol Oncol. 2019;41(2):129-132. Lobbes H. Pure red cell aplasia: Diagnosis, classification and treatment. Rev Med Interne 2023; 44 (1): 19-26

Anemia emolitica autoimmune (AHIA) In caso di fallimento della terapia immunosoppressiva	PDN, RTX	In emergenza (o nei bambini con EPN) IVIg 0.4-0.5g/kg per 2-5 gg (1 ciclo)	Hill QA, Stamps R, et al. Guidelines on the management of drug-induced immune and secondary autoimmune, haemolytic anaemia. Br J Haematol 2017; 177:208–20. Marina MA, Lopez Rubio M, Garcia LC. Autoimmune haemolytic anaemia. Med Clin 2023; 160(1): 30-38
Emofilia autoimmune acquisita	Prima linea Corticosteroidi o combinazione di corticosterodi + ciclofosfamide. Seconda linea Rituximab	Terza linea: IVIg 0.4-0.5g/kg per 2-5 gg per 1 ciclo, poi rivalutazione	Franchini M, Vaglio S, et al. Acquired hemophilia A: a review of recent data and new therapeutic options. Hematology 2017; 22:514–20. Tiede A, et al. International recommendations on the diagnosis and treatment of acquired emophilia A. Haematologica 2020; 105(7):1791-1801.
Infezione successivaa BMT o HSCT	Antibiotici, antivirali, antifungini	Terapia di supporto: IVIg 0.4-0.5g/kg per 2-5 gg per 1 ciclo	Di Cristanziano V, Affeldt P, et al. Combined Therapy with Intravenous Immunoglobulins, Letermovir and (Val-) Ganciclovir in complicated courses of CMV-Infection in Transplant recipients. Microorganism 2021; 9(8):1666.
Malattia di von Willebrand acquisita	Trattamento della condizione di base; desmopressina, fattore VIII/vWD, plasma exchange	IVIg 0.4-0.5g/kg per 2-5 gg (1 ciclo) nella aVWS associata a gammopatia monoclonali MGUS IgG	Lavin M, Ryan K, et al. A role for intravenous immunoglobulin in the treatment of Acquired Von Willebrand Syndrome associated with IgM gammopathy. Haemophilia 2018; 24:e22– 5.118. Nguyen A, Repesse Y, et al. IVIG increases interleukin-11 levels, which in turn contribute to increased platelets, VVF and FVIII in mice and Humans. Clin Exp Immunol 2021; 204:258-66. Langer AL, Connell NT. Acquired von Willebrand Syndrome. Haematol Oncol Clin North Am 2021; 11:S0889-8588(21)000084-8. Ghariani I, Braham N, Veyradier A, Bekir L. Acquired von Willebrand syndrome: five cases report and literature review Thromb Res 2022; 218: 145-150
Sindrome emofagocitica / Linfoistiocitosi emofagocitica (HLH) in caso di infezioni ricorrenti	Corticoster oidi, Etoposide	IVIg 0.4-0.5g/kg per 2-5 gg/mese (1 ciclo, ripetibile ogni mese)	Case reports di HLH dopo infezione virale(EBV, SARS-CoV-2)
		NEUROLOGIA	
ADEM / gruppo della neuromielite ottica dell'età pediatrica (NMOSD)	Corticosteroidi, plasma exchange	In età pediatrica: IVIg 2 g/kg (max 80 g) a cadenza mensile	Hacohen Y, Banwell B. Treatment Approaches for MOG-Ab-Associated Demyelination in Children. Curr Treat Options Neurol 2019;21:2. Matricardi S, Farello G, Savasta S, Verrotti A. Understanding childhood neuroimmune diseases of the central nervous system. Front Pediatr 2019;5:511.
ADEM Multifasica (MDEM) dell'età pediatrica	Corticosteroidi, plasma exchange	In età pediatrica: IVIg 2 g/kg (max 80 g) a cadenza mensile	Matricardi S, Farello G, Savasta S, et al. Understanding childhood neuroimmune diseases of the central nervous system. Front Pediatr 2019;5:511.
Disordini dello spettro della neuromielite ottica (NMOSDs) dell'età	Corticosteroidi, plasma exchange, immunosoppres-	In età pediatrica: IVIg 2 g/kg (max 80 g) a cadenza mensile	Matricardi S, Farello G, Savasta S, et al.Understanding childhood neuroimmunediseases of the central nervous system. Front Pediatr 2019;5:511.

pediatrica (anticorpi anti-AQP4; anticorpi anti-MOG; sieronegativi)	sori, anticorpi monoclonali		
Sindrome clinicamente isolata (CIS) dell'età pediatrica	Corticosteroidi, plasma exchange	In età pediatrica: IVIg 2 g/kg (max 80 g) a cadenza mensile	Matricardi S, Farello G, Savasta S, et al. Understanding childhood neuroimmune diseases of the central nervous system. Front Pediatr 2019;5:511.
Sindrome opsoclono-mioclono in età pediatrica	Corticosteroidi, immunosoppres-sori, anticorpi monoclonali	In età pediatrica: IVIg 2 g/kg (max 80 g) a cadenza mensile	Pranzatelli M, Tate ED. Dexamethasone, Intravenous Immunoglobulin, and Rituximab Combination Immunotherapy for Pediatric Opsoclonus-Myoclonus Syndrome. Pediatr Neurol 2017;73:48-56. Blaes F, Dharmalingam B. Childhood opsoclonus-myoclonus syndrome: diagnosis and treatment. Expert Rev. Neurother;16(6):641-8
DERMATOLOGIA			
Pyoderma gangrenosum	Immunosoppres sori	IVIg 0.4-0.5g/kg per 2-5 gg per 1 ciclo, poi rivalutazione	Cummins DL, Anhalt GJ, et al. Treatment ofpyoderma gangrenosum with intravenous immunoglobulin. Brit J Dermatol2007;157:1235–1239. Emre S. Intravenous immunoglobulin treatment: Where do dermatologists stand? Dermatol Ther 2019; 32:e12854. AU Song H, Lahood N, Mostaghimi, et al. Intravenous immunoglobulin as adjunct therapy for refractory pyoderma gangrenosum: systematic review of cases and case series. Dermatol. 2018;178(2):363.
PEDIATRIA			
Colite severa o ricorrente da C. difficile	Antibiotici, colectomia	IVIg 0.4-0.5g/kg per 2-5 gg/ per unciclo	Joseph J, Singhal S, et al. Clostridium difficile colitis: review of the therapeutic approach. Am J Ther 2014; 21(5):385-94.
Disturbi del movimento post-infettivi (Corea di Sydenham, atassia cerebellare acuta, ecc…)	Corticosteroidi	IVIg 2 g/kg (max 80 g)	Nosadini M, Mohammad SS, Suppiej A, et al. IVIG in Neurology Study Group. Intravenous immunoglobulin in paediatricneurology: safety, adherence to guidelines, and long-term outcome. Dev Med Child Neurol 2016;58(11):1180- 1192.
Encefalite di Rasmussen	Farmaci anticrisi, corticosteroidi, immunosoppress ori, anticorpi monoclonali, emisferotomia	IVIg 2 g/kg (max 80 g) a cadenza mensile	Varadkar S, Bien CG, Kruse CA, et al. Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet Neurol 2014;13(2):195-205.
Epilessia intrattabiledel bambino	Terapia antiepilettica combinata	IVIg 2 g/kg (max 80 g) a cadenza mensile	Geng JS, Dong JC, Li Y, et al. Intravenous immunoglobulins for epilepsy. Cochrane Database of Systematic Reviews 2019, Issue 12, Art. No.: CD008557. Fauzi AA, Engkasan PJ. What are the effectsof IVIg on seizures and quality of life of people with epilepsy? A Cochrane Review summary with commentary. Dev Med Child Neurol 2021;63(5):501-502.
Malattia emoliticadel neonato	Per il neonato: in caso di	IgEV 0.5-1 g/kg dose ripetibile se necessario	Am Acad Ped. Subcommittee on Hyperbilirubinemia Management of hyperbilirubinemia in the newborn

	iperbilirubinemia da allo-immunizzazione materna, se fallimento della fototerapia e la exsanguino-trasfusione non può essere effettuata in tempi ragionevoli		infant 35 or more weeks of gestation. Pediatrics 2004, 114, 297. Zwiers C. Scheffer-Rath MEA. Lopriore E, etal. Immunoglobulin for alloimmune hemolytic disease in neonates. Cochrane Database Syst. Rev. 2018
PANDAS (disordine neuropsichiatrico autoimmune pediatrico associatoa infezione streptococcica) PANS (Pediatric Acute-onset Neuropsychiatric Syndrome)	Non stabilito Neurolettici, corticosteroidi	IVIg 2 g/kg (max80 g)	Johnson M, Ehlers S, et al. Anti- inflammatory, antibacterial, and immunomodulatory treatment in children with symptoms corresponding to the research condition PANS (Pediatric Acute- onset Neuropsychiatric Syndrome): A systematic review. PLoS One 2021;16(7):e0253844. Melamed I, Kobayashi RH, et al. Evaluation of Intravenous Immunoglobulin inPediatric Acute-Onset Neuropsychiatric Syndrome. J Child Adolesc Psychopharmacol 2021;31(2):118-128.
Patologie autoinfiammatorie genetiche (es. Aicardi–Goutières syndrome)	Corticosteroidi, immunosoppres sori	IVIg 2 g/kg (max80 g) a cadenza mensile	Nosadini M, Mohammad SS, Suppiej A, al. IVIG in Neurology Study Group. Intravenous immunoglobulin in paediatric neurology: safety, adherence to guidelines, and long-term outcome. Dev Med Child Neurol 2016;58(11):1180- 1192. Matricardi S, Farello G, Savasta S, Verrotti A. Understanding childhood neuroimmune diseases of the central nervous system. Front Pediatr 2019;5:511.
		TRAPIANTI	
Trattamento di infezioni virali (polmonite, retinite) dopo trapianto di organo solido	Antivirali	Non indicate di routine	Majeed A, Latif A, et al. Resistant Cytomegalovirus Infection in Solid-organTransplantation: Single-center Experience, Literature Review of Risk Factors, and Proposed Preventive Strategies. TransplantProc. 2018; 50(10):3756-3762. Fu L, Santhanakrishnan K, et al. Management of Ganciclovir Resistant Cytomegalovirus Retinitis in a Solid Organ Transplant Recipient: A Review of Current Evidence and Treatment Approaches. Ocul Immunol Inflamm 2020; 28(7):1152-1158. Barten MJ, Baldanti F, Staus A, et al. Effectiveness of Prophylactic Human Cytomegalovirus Hyperimmunoglobulin in Preventing Cytomegalovirus Infection following Transplantation: A Systematic Review and Meta-Analysis. Life (Basel). 2022;12(3):361.
		OFTALMOLOGIA	
Malattia di Graves	Corticosteroidi, Immunosoppres-sori altri	Nei casi refrattari. IVIg 0.4-0.5g/kg per 2-5 gg/mese per 3 mesi, poi rivalutazione	Fallahi P, Ferrari SM, et al. Cytokines as Targets of Novel Therapies for Graves' Ophthalmopathy. Front Endocrinol (Lausanne). 2021; 12: 654473.
Retinite da CMV dopo trapianto diorgano	Antivirali	Non indicate di routine	Fu L, Santhanakrishnan K, et al. Management of Ganciclovir Resistant Cytomegalovirus Retinitis in a

solido			Solid Organ Transplant Recipient: A Review of Current Evidence and Treatment Approaches. Ocul Immunol Inflamm 2020; 28(7):1152-1158. Limaye AP, Babu TM, Boeckh M. Progress and Challenges in the Prevention, Diagnosis, and Management of Cytomegalovirus Infection in Transplantation. Clin Microbiol Rev. 2020;34(1):e00043-19.
Uveite autoimmune	Corticosteroidi, Immunosoppres -sori, altri	Nei casi refrattari. IVIg 0.4-0.5g/kg per 2-5 gg/mese per 3 mesi, poi rivalutazione	Saadoun D, Bodaghi B, et al. Biotherapies in inflammatory ocular disorders: IFN, Ig, MonoAb. Autoimmun Rev. 2013; 12(7):774-83. Feurer E, Bielefeld P, Saadoun D, et al. Uvéites et biothérapies [Biologics in uveitis]. Rev Med Interne. 2015;36(2):107-16.