First author, year	Centre	Population	Prevalence of AIC	Prevalence of AIHA	Onset time post HSCT (median, range)	Risk factors-univariate analysis	Risk factors-multivariate analysis	Survival	Comments
Drobyski, 1996[60]	Single centre, Wisconsin, USA	Adults, 236 T cell depleted HSCT	Not reported	2.9%	10 months (7-25 months)	Not reported	Not reported	4/7 died of infectious complications or AIHA complication	
Chen, 1997[61]	Single centre, UK	Adults, 293 HSCT	Not reported	3.1%	wAIHA 6-18 months, cAIHA 2-8 months	Not reported	Not reported	5/9 died, none of AIHA	2/4 cAIHA had no clinically evident haemolysis
Horn, 1999[1]	Single centre, San Francisco, USA	Children with SCID, 41 haplo (T depleted) HSCT	Not reported	19.5%	Not reported	PBSC as source of stem cell	PBSC as source of stem cell	1/8 died at presentation, 3 of infections (2 with active haemolysis)	Abnormal T cell reconstitution and function in >70% of patients with AIHA.
O'Brien, 2004[26]	Single centre, Minnesota, USA	Children, 439 HSCT	Not reported	Prevalence: 4.3% 1-year CI 4%, 3-year CI 5%	4 months (2–32 months)	Age <10 years, metabolic disease	Metabolic disease	10/19 died, 3 because of AIHA, 5 of infection during AIHA treatment	All cases of AIHA occurred in MUD HSCT.
Sanz, 2007[24]	Single centre, Spain	Adults, 272 HSCT for haematological malignancies	Not reported	3-year CI 4.4%	147 days (41–170)	HLA mismatch, unrelated donor, extensive cGVHD, UCBT	Unrelated donor, extensive cGVHD	10/12 died	
Page, 2008[2]	Single centre, Duke University, USA	19 UCBT in children with metabolic disorders (1 with thalassemia)	2-year CI 56%	21%	AIC: 247 days (92-687)	Infants compared to older children	Not reported	5-year OS 80% (entire cohort)	High T cell dose in UCB could account for GVHD and immune dysregulation
Daikeler, 2013[22]	Multicentre, Eurocord	Adults and children, 778 UCBT	5-year CI of AID 6.6%, most frequently AIC	2.5%	AID: 191 days (27-4267)	For all AID: age <15 years, diagnosis of non-malignant disease, HLA match ≥5/6, no TBI conditioning, interval from diagnosis to UCBT <11.4 months	Risk factors for AID: diagnosis of non-malignant disease and interval from diagnosis to UCBT <11.4 months	5-year OS was 59% for AIHA, 67% for Evans syndrome, 91% for ITP. 6/52 died of AIC (2 AIHA).	8% mixed chimerism in patients with AID (same as in control group).
Faraci, 2014[27]	Multicentre, Italy	Children, 1574 HSCT	3-year CI 2.13 %, 10-year CI 2.5%	10-yr CI 1.5%	AIHA 5.2 months (1.3 - 100.9)	For all AIC: younger age, HSCT from alternative donor, primary non-malignant disorder, UCBT	alternative donor, primary non-malignant disorder	85%	87% achieved remission with Rtx (100% in AIHA)

Sanz, 2014[31]	Single centre, Spain	Adults, 281 single UCBT for haematological malignancies	3-year CI 6.8%	3-year CI 5.4%	AIHA: 181 days (25-543)	cGVHD, diagnosis of CML	cGVHD, diagnosis of CML	10/15 died: 6 of infections, 1 of AIHA (massive haemolysis), 1 of relapse, 1 of GVHD, 1 of 2nd tumor	AIC has high mortality. RTX should be considered upfront
Ahmed, 2015[30]	Single centre, Texas, USA	Children, 500 1st HSCT, 72 2nd HSCT	Not reported	2.4% after 1st HSCT, 9.7% after 2nd HSCT	273 days (119–4505 days) after 1st HSCT, 157 days (70 –256 days) after 2nd HSCT	Matched related donor reduces the risk of AIHA. No other risk factors confirmed	Not reported	No difference in survival between patients with AIHA or without	4 received 2nd HSCT as treatment for AIHA, 3 out of 4 unsuccessfully.
Wang, 2015[5]	Single centre, London, UK	Adults, 533 HSCT	Not reported	3.6%	202 days	Unrelated donor, concordant gender recipient/donor	Unrelated donor	CR in 47%, PR 32%. Alive: 9/19, 4 died of AIHA	AIHA was associated with increased overall mortality (HR 2.48) and increased TRM (HR 4.38)
Bhatt, 2016[32]	Single centre, New York, USA	Adults and children, 152 double UCBT	3-year CI 7%	5.2%	AIC: 10.4 months (range 5.8–24.5)	Not reported	Not reported	9/10 alive, 8/10 in remission of AIC	All full donor chimerism. All AIC occurred during IS weaning. Most patients (8/10) had cGHVD. Steroids + early RTX are suggested
Chang, 2016[34]	Single centre, Taiwan	Children, 265 HSCT	Not reported	5.6%	Not reported	Not reported.	Not reported	12/15 achieved CR, 2/15 refractory	Among AIHA: 12/15 received UCBT, 13/15 had cGVHD, 9/15 had a diagnosis of thalassemia.
Hwang-Bo, 2017[62]	Single centre, Korea	Children, 292 HSCT	2.4%	0.7%	AIC: 3.6 months	Not reported	Not reported	All alive at median 27 months after HSCT	All pts with AIC received ATG and MUD donor.
Lv, 2017[63]	Single centre, China	Adults, 445 HSCT	3-yr CI 4.0%	1.3%	AIC: 196 days (60 to 756 days)	For all AIC: haplo-HSCT, source of stem cell, HLA disparity, cGVHD.	Haplo-HSCT, cGVHD.	3-year OS 83.3% at a median 355.5 days (range, 2–1464 days) post AIC	
Kruizinga, 2018[21]	Single centre, the Netherlands	Children, 531 HSCT	3-yr CI 5%	2.2%	AIC: 5 months (1-36)	For all AIC: non-malignant disorder, CMV reactivation, non-TBI conditioning	Non-malignant disorder, CMV reactivation, Alemtuzumab	79%	TH2 shifted cytokine profile in patients with AIC. Bortezomib and Sirolimus are promising
Gonzalez-Vicent, 2018[16]	Multicentre, Spain	Adults and children, 4099 HSCT	Not reported	1.5%	6 months (1-55 months)	Age <15 years, UCBT, MMUD	Not done	CI of AIHA related mortality is 17%.	DFS 52% (at 40 months).

									Age <15 years and response to treatment have better DFS. Steroids +RTX should be offered upfront.
Deambrosis, 2019[3]	Single centre, Manchester UK	Children with Hurler syndrome, 36 UCBT	22%	8.3%	AIC: 66 days (range, 22-96 days)	For all AIC: higher pre-transplant absolute lymphocyte count and FluBu conditioning	Higher pre-transplant absolute lymphocyte count	One death, 2 episodes of life threatening bleeding. 2 pts experience subsequent graft rejection	In 3 cases anti-RBC AB were of recipient origin. Hypothesis: inadequate recipient immunosuppression in FluBu-conditioned AIC.
Neely, 2019[19]	Single centre, San Francisco, USA	Children, 442 HSCT	4.5%	2.0%	AIC: 5.2 months (1.5-15.1)	For all AIC; older age. In patients with malignancies, no T cell recovery at time of AIC.	Not done	Higher mortality among AIC compared to controls (15% vs 7%).	40% mixed chimerism at AIC onset.
Scordo, 2019[42]	Single centre, New York, USA	Adults, 408 CD34+ selected HSCT for haematological malignancies	3-year CI 5.8%	2.4%	AIC: 189 days (39 -840)	Diseases risk index>3		1 patient died of AIHA. 6-month OS after AIC 74%.	AIC is not a risk factor for NRM but increases relapse.
Lv, 2019[25]	Multicentre, China	Adults, 1377 HSCT for haematological malignancies	Not reported	3-year CI 2.2%	215 days (34-756)	Haplo-HSCT, HLA mismatch, cGVHD, ATG	Haplo-HSCT, cGVHD		All full donor chimerism. Patients with AIHA have lower rate of relapse, higher DFS and OS
Szanto, 2020[20]	Single centre, the Netherlands	Children, 380 HSCT	5-year CI 7.8%	6.3%(mostly Evans)	AIC: 133 days (46 – 445)	For all AIC: UCBT, aGVHD grade II-IV, serotherapy, no chemotherapy before HSCT.	All AIC: aGVHD grade II-IV, serotherapy, no chemotherapy before HSCT.	OS 83%	All full donor chimerism. AIC patients have lower T and NK and increased IgA, IgM, and IgG
Miller, 2020[29]	Multicentre, EBMT	Adults and children with AA, 530 HSCT	5-year CI 4.6%	1.3%	AIC: 10.6 months (2.6–91.5)	For all AIC: Alemtuzumab, RIC, PBSC	All AIC: RIC, PBSC	5 year OS 85.9%. 2 died of infection with AIC not in remission	
Lum, 2020[28]	Single centre, Newcastle, UK	Children with primary immunodeficiency, 502 HSCT	5-year CI 9.4%	3.7%	AIC: 6.5 months (2.5 months to 18.2 years)	For all AIC: pre-HSCT AIC, MMUD, Alemtuzumab, ATG, aGVHD g II-IV, cGVHD	Alemtuzumab	5 year TRM 12 % at median 5.8 years	RIC associated with the need for >2 line of therapy
Koo, 2020[18]	Single centre, USA	Children, 354 HSCT	5.6%	3.6%	AIC: 219 days (range, 97-1205 days)	MMUD.		Only 25% of patients had a CR with initial therapy	Mixed chimerism is not a risk factor.

									High prevalence of steroid related side effects (AVN, cataract) and hypogammaglobulinemia post RTX.

Table I: Summary of relevant studies reporting incidence and risk factors of post-HSCT AIHA.

Abbreviations: 6-MP 6-mercaptopurine, AA aplastic anaemia, AB antibody, aGVHD acute graft versus host disease, AIC autoimmune cytopenia, AID autoimmune disease, AIHA autoimmune haemolytic anaemia, ATG anti-thymocyte globulin, AVN avascular necrosis, cAIHA cold autoimmune haemolytic anaemia, cGVHD chronic graft versus host disease, CI cumulative incidence, CML chronic myelocytic leukaemia, CR complete remission, CSA cyclosporine, DFS disease free survival, EBMT European society for Blood and Marrow Transplantation, FluBU Fludarabine Busulphan, GVHD graft versus host disease, haplo haploidentical, HLA human leukocyte antigen, HR hazard ratio, HSCT haematopoietic stem cell transplantation, IS immune-suppressive, ITP immune thrombocytopenia, IVIG Intra-venous Immunoglobulin, MMF mycophenolate mofetil, MMUD mismatched unrelated donor, MP methylprednisolone, MSD matched sibling donor, NRM non-relapse mortality, OS overall survival, PBSC peripheral blood stem cells, PR partial remission, RBC red blood cell, RIC reduced intensity conditioning, RTX Rituximab, SCID severe combined immune-deficiency, TBI total body irradiation, TRM transplant related mortality, UCBT umbilical cord blood transplantation, UK United Kingdom, USA United States of America, wAIHA warm autoimmune haemolytic anaemia