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The Italian registry of therapeutic apheresis in SISTRA: Year of activity 2023

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ABSTRACT

The Italian Registry of Therapeutic Apheresis (IRTA) collects clinical data on patients undergoing therapeutic apheresis procedures throughout the national territory, with the main objective of improving the quality and safety of the care provided to the patient. Given the importance of centralizing the collection and analysis of information on therapeutic apheresis, the National Blood Center (NBC), at the request of the Italian Scientific Society of Hemapheresis and Cellular Manipulation (SIdEM), has included IRTA in the Information System of Transfusion Services (SISTRA), which is the information system of the Ministry of Health for the exchange of data on blood and its derivatives between the Italian Regions and the NBC. This manuscript reports IRTA activity data for 2023 maintaining the general approach introduced in previous manuscripts to facilitate comparison with already published activity data (2020–2022). For each therapeutic apheresis procedure (more than 15) we reported the number of procedures, the number of patients treated, and adverse effects. Furthermore, for each pathology belonging to more than 8 specialized clinical areas we reported the number of procedures, the number of patients treated, the number of patients at first diagnosis and the outcome of the patients. More than 36000 procedures in more than 8500 patients were included in the 2023 database. The aim of the IRTA 2023 activity data is to provide an updated snapshot of the use of therapeutic apheresis in the treatment of human diseases in Italy and a strategic resource for institutions and scientific societies.

1. Introduction

Apheresis refers to the process of separating the cellular and soluble components of blood and may be used therapeutically to treat various disorders or to collect cells for cellular therapies such as hematopoietic stem cell therapy and chimeric T-cell antigen receptor (CAR-T) therapy.

The IRTA, or the Italian Registry of Therapeutic Apheresis, was established 25 years ago on the initiative of the Italian Scientific Society of Hemapheresis and Cellular Manipulation (SIdEM). It collects data on therapeutic apheresis procedures performed in Italy with the aim of obtaining more information on outcome data and side effects and to facilitate the transfer of methods and knowledge. In 2019 the National Blood Center (NBC), at the request of the Italian Scientific Society of Hemapheresis and Cellular Manipulation (SIdEM), included IRTA in the Information System of Transfusion Services (SISTRA) [1] which allows the exchange of information flows between the Ministry of Health, the NBC, the transfusion services of the Regions, the autonomous provinces of Trento and Bolzano and the armed forces and whose activity is coordinated by the NBC. The purpose of this report is to provide an update on IRTA registry data.

2. Material and methods

Participation in data collection is voluntary and participants enter data annually. The cumulative annual data are entered into the IRTA from January to April of the year following the survey by the contact person of the Therapeutic Apheresis (TA) apheresis center who has obtained access to the SISTRA registry on the website https://cns.sanita.

Abbreviations: NBC, the Italian National Blood Center; SIdEM, the Italian Scientific Society of Hemapheresis and Cell Manipulation; SISTRA, the Information System of Transfusion Services; IRTA, the Italian Registry of Therapeutic Apheresis, TA Therapeutic Apheresis, ASFA American Society for Apheresis.

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it/SISTRA/. Data are checked for significant outliers or implausible data by the registry manager. The types of procedures and the related pathologies are identified by a specific code generated by SISTRA. No personal data is recorded. Emergency procedures include not only plasmaexchange, but also photopheresis procedures provided in the treatment of cellular rejection of solid organ transplants, particularly liver and lung. The autologous collection of peripheral stem cells also constitutes an emergency in the case of pediatric patients, as already reported in the literature [2]. A descriptive analysis of the collected data has been perfomed.

3. Results

Out 139 therapeutic apheresis centers accredited in SISTRA, 110 (+79 %) entered their data. This participation is in line with 2022 data. During the 2023 year, a total of 36208 procedures were performed in 8596 patients. The most common TA procedure performed (Table 1) was therapeutic plasma exchange which accounted for 43.4 % (+10.5 % vs. 2022) followed by extracorporeal photopheresis 26.6 % (+0.6 % vs 2022), erythrocyte exchanges 7.6 % (+9.9 % vs. 2022), erythro-apheresis 8.3 % (−18.5 % vs. 2022), autologous hematopoietic stem cells collections 11.9 % (−1.9 % vs. 2022), and lipoprotein removal procedures 1.9 % (+12.8 % vs 2022) (Table 1). Among the selective procedures, cascade filtration procedures accounted for 1.7 % (+4.5 % vs. 2022), plasma-adsorption procedures for 0.3 % (+35.8 % vs 2022) and immunoadsorption procedures for 0.1 % (−10.3 % vs. 2022).

537 procedures do not fall under any of the types provided for in the register and have been referred to as "other". Analyzing the data, most of these are lymphocytoapheresis procedures for Car-T: 287 collection procedures in 274 patients, 57 of them pediatric (Table 1).

The indication for the use of a specific procedure is linked to the pathogenetic mechanism underlying the disease or to the clinical picture of the patient. As reported in the literature, and foreseen by the American ASFA guidelines [3], plasmapheresis is mainly used in diseases with humoral immunological pathogenesis, while photochemotherapy is indicated when the alteration of the immune system involves the lympho-monocyte cellular component.

Adverse events occurred in 890 procedures, 2.5 % of the total procedures (−4.3 % vs 2022) The most of them were mild and predominantly referred to hypocalcemia which represents 47.7 % of all adverse events. Severe adverse events as described in Table 2 represented 1 % of all adverse events and occurred during therapeutic plasma exchange (7 events) and peripheral stem cell collection (2 event) (Table 2).

Table 2
Adverse events to therapeutic apheresis procedures.

Therapeutic procedure	Mild *	Moderate	Severe **
1 – Therapeutic plasma exchange	401	29	7
2 - Cascade filtration	3	0	0
3 - Plasma adsorption (physical, chemical)	0	0	0
4 - IgG / IgE Immunoadsorption	0	0	0
5 – Extracorporeal photopheresis (online)	21	0	0
6 – Extracorporeal photopheresis (off line)	38	1	0
7 - Lipoprotein apheresis	9	2	0
8 - Lymphoplasmapheresis	0	0	0
9 - Cytoreductive leukapheresis	0	0	0
10 - Granulocyte-monocytoapheresis	32	0	0
11 - Therapeutic platelet apheresis	0	0	0
12 - Erythrocyte exchange	54	0	0
13 – Erythro-apheresis	11	0	0
14 – Haematopoietic Stem Cell Collection (HSCC-autotransplant)	269	8	2
15 - Other	3	0	0
Total	**841**	**40**	**9**

Moderate: allergic/hypersensitivity reactions, digestive disorders, nausea/vomiting, fever and chills, general discomfort;
* **Mild**: hypocalcemic symptoms, blood circuit clotting, hematoma at puncture site, insufficient blood flow rate;
** **Severe**: cardiovascular collapse, vaso vagal reaction/fainting, hemolysis, arrhythmias, use of resuscitation maneuvers.

Table 3 shows the number of hematopoietic stem cell collection, cytoapheresis and photopheresis procedures. The collection of autologous peripheral blood hematopoietic stem cells was carried out in 2624 patients (−4.2 % vs 2022), with an average of 1.5 procedures per patient, indicating the good timing of the collection and the efficiency of cell separators. Our data confirm that the pheripheral blood is the major source of hematophoietic stem cells finalized to the autologous transplantation in myeloma and lymphoma patients. Notably, erythrocyte exchange applies mainly to sickle cell disease whereas erythro-apheresis applies to polycythemia/erythrocytosis. Extracorporeal photopheresis is mainly used in the treatment of GvHD in organ transplant rejection and cutaneous T-cell lymphoma. Its use in autoimmune diseases is still limited, with only 8 patients treated and 71 procedures (Table 3).

As reported in the reference guidelines of the American Society of Apheresis (ASFA, 2023) [3], the specialty areas of application of therapeutic apheresis are numerous. The 2023 IRTA data indicate that the

Table 1
Therapeutic apheresis procedures and number of treated patients, including paediatric patients and emergency procedures.

Therapeutic procedure	Procedures (including emergency procedures) (n)	Patients (including paediatric patients) (n)	Paediatric patients (n)	Emergency procedures (n)
1* – Therapeutic plasma exchange	15064	2277	85	1032
2* - Cascade filtration	596	89	0	1
3* - Plasma adsorption (physical, chemical)	109	13	2	0
4* - IgG / IgE Immunoadsorption	39	5	0	0
5* – Extracorporeal photopheresis (online)	4525	292	12	6
6* – Extracorporeal photopheresis (off line)	4695	739	23	7
7* - Lipoprotein apheresis	670	28	3	0
8* - Lymphoplasmapheresis	2	2	0	0
9* - Cytoreductive leukapheresis	64	39	4	26
10* - Granulocyte-monocyte-apheresis	195	27	0	0
11* - Therapeutic platelet apheresis	40	19	0	2
12* - Erythrocyte exchange	2652	520	78	100
13* - Erythro-apheresis	2885	1343	1	40
14* – Autologous Stem Cell Collection	4135	2817	138	83
15* - Other	537	386	57	0
Total	**36208**	**8596**	**403**	**1297**

* The number refers to an internal code generated by SISTRA

Table 3
Haematopoietic Stem Cell collection (HSCC), Cytoapheresis and Photopheresis: number of procedures and number of patients by disorders.

HSC Collection	Procedures (n)	Patients (n)
700* - Multiple myeloma	2168	1313
701* - Lymphoma	1196	976
702* - Acute leukaemia (Autograft/Back up)	126	92
703* - Neuroblastoma	67	46
704* - Other solid tumour	181	131
799* - Other	91	66
Total	**3829**	**2624**
Cytoapheresis	**Procedures (n)**	**Patients (n)**
710* - Sickle Cell Disease (Erythrocyte Exchange)	2122	376
711* - Malaria (Erythrocyte Exchange)	0	0
712* - Polycythaemia / Erythrocytosis (Erythro-apheresis)	1436	660
713* -Acute Myeloid Leukemia (AML) (cytoreductive leukapheresis)	29	22
714* - Acute lymphoblastic Leukemia (ALL) (cytoreductive leukapheresis)	8	5
799* - Other	232	94
Total	**3827**	**1157**
Photopheresis	**Procedures (n)**	**Patients (n)**
720* - GVHD-Graft versus Host Disease	5946	402
721* - Rejection of solid organ	1136	125
722* - Cutaneous T lymphoma / Sezary syndrome	617	56
723* - Autoimmune diseases	71	8
799* - Other	25	3
Total	**7795**	**594**

* The number refers to an internal code generated by SISTRA.

apheresis procedures were mainly used in haematology with 9197 procedures (−15.3 % vs. 2022) in 1895 patients (−21.2 % vs 2022), followed by neurology, with 7250 procedures (+3.8 % vs 2022) in 1155 patients (+7.5 % vs 2022), and solid organ transplantation with 1894 procedures (−4.2 % vs 2022) in 262 patients (+14.9 % vs 2022) (Table 4).

In haematology, the main diseases treated were polycythemia vera (erythro-apheresis, category I, grade recommendation 1B according to the 2023 ASFA Guidelines) (−31.7 % vs 2022) followed by GvHD (−21.7 % vs 2022) (ECP, category II, grade 1B), Sickle Cell Disease, non-Acute (−1.1 % vs 2022) (RBC exchange, category I, II and III, grade 1 A, 2 A and 2B), and Thrombotic thrombocytopaenic purpura (TPE, category I, grade 1 A) (−26.4 % vs 2022) (Table 5). Only in approximately 1 % of hematological patients the clinical indication included category III, grade of recommendation 2 C, confirming the high level of appropriateness; also the patients treated for haematological diseases, not included in the ASFA Guidelines, do not exceed 1 %.

In patients with polycythemia vera 1858 procedures were performed in 838 patients (−31.7 % vs 2022) with an average of 2.2 procedures/patient. A favorable response (remission 8, improved 446) was observed in 94.9 % of the 478 patients evaluated.

The largest number of procedures was performed for the treatment of GvHD, with 3306 in 235 patients and an average of 14 procedures/patient. We evaluated 209 patients and found that 16.7 % of those achieved the remission of the clinical picture (Table 5).

Table 4
Specialty areas of therapeutic apheresis use, number of patients and procedures.

	Procedures (n)	Patients (n)
Haematology	9197	1895
Neurology	7250	1155
Solid Organ Transplant	1894	262
Metabolism	871	73
Rheumatology	864	134
Nephrology	643	56
Dermatology	513	48
Gastrointestinal System	165	36
Other	32	9

Therapeutic apheresis also was a widely used therapy in thrombotic thrombocytopenic purpura with 1225 procedures in 162 patients and an average of 7.6 procedures/patient. The outcome, available for 135 of these patients, was 96.3 % of positive responses with 77 % remissions of the clinical picture and 19.3 % improvements.

The response to the treatment of inherited haemochromatosis was equally positive. Out of 71 patients treated, whose outcome was reported, 100 % had a positive response.

The overall outcome for the haematological disorders was available for 1399 patients (73.8 %) with 269 remissions of the clinical picture (19.3 %) and 1022 improvements (73 %) (Table 5).

Of note, 5.5 % of patients were registered in the "Other" group of hematological diseases, that is patients whose pathology does not fall within those indicated in the ASFA 2023 Guidelines.

In Table 6 we report the use of therapeutic apheresis procedures in neurological diseases. Myasthenia (2740 treatments, −2.4 % vs 2022), chronic inflammatory demyelinating polyneuropathy (CIDP) (1441 treatments, +1.6 % vs 2022) and Guillain-Barré syndrome (GBS) (1303 treatments, +10.2 % vs 2022) are the most frequent diseases where therapeutic apheresis was used. From the analysis of the available outcome data, the best response was for myasthenia (83.9 %) followed by GBS (82.3 %), and CIDP (66.5 %). These are pathologies for which the indication for apheresis has a high level of appropriateness; in fact, only in approximately 2 % of neurological treated patients the ASFA indication fell into category III, grade 2 C; among these the most represented disease is Stiff Man Syndrome.

By analyzing the outcome data, an improvement or remission of the clinical picture was observed in 74 % of the evaluated patients, most of whose were on maintenance therapy or recovering from disease flares. The outcome was available for 958 patients (83 % of total) (+6.4 % vs 2022): of these, 90 are in remission of the clinical picture (9.4 % of total) (−23.7 % vs 2022) and 621 show improvement (65 % of total) (+4.5 % vs 2022. Only 4.2 % of the treated patients had a pathology not covered by the ASFA Guidelines (Other category).

In rheumatology (Table 7), the main diseases treated were vasculitis, ANCA-associated glomerulonephritis and cryoglobulinemia. Vasculitis was observed in 38 patients who were treated with 264 procedures (6.9 procedures/patient) (+8 % vs 2022). Most of these patients experienced an improvement (71.8 %) or stabilization of the clinical picture (12.5 %). Disease remission was observed in 6.3 % of patients.

In 28 patients with cryoglobulinemia, 225 procedures were performed with an average of 8 treatments per patient. Improvement of the clinical picture was obtained in 11 patients and remission in 4.

On the whole, the outcome data were available for 104 patients (77.6 %) with only 14 remissions of the clinical picture and 62 improvements (59.6 %).

The third most represented pathology is ANCA-associated glomerulonephritis, included in the new ASFA guidelines as Mycroscopic polyangiitis and Granulomatosis with polyangiitis. These 21 patients were treated with 117 procedures with an average of 5.6 treatments per patient. Outcome data were available for 17 patients of which 11 (64.7 %) had an improvement and 2 (11.7 %) remission. Approximately 12.7 % of the treated patients had a pathology not covered by the ASFA Guidelines (Other category).

In the field of organ transplantation (Table 8), 1894 treatments were performed in 262 patients, with 7.2 procedures per patient. The largest number of treatments was in patients with lung transplant-bronchiolitis obliterative syndrome (BOS) (8.8 procedures/patient), heart transplant-recurrent rejection, (12.7 procedures/patient), and ABO compatible kidney transplant-Ab mediated rejection (5.2 procedures per patient).

The therapeutic apheresis as supportive therapy in solid organ transplantation is still not supported by an adequate number of randomized controlled studies, and many experimental aspects remain

Table 5
Haematological disorders: number of procedures, number of treated patients, number of patients at first diagnosis and patients' outcome.

HAEMATOLOGY	Procedures (n)	Patients (n)	Patients at first diagnosis (n)	Patients' outcome			
				Remission	Improved	Unchanged	Worsened
17 - Systemic amyloidosis	7	4	1	0	1	0	0
18 - Autoimmune haemolytic anaemia- Cold agglutinin disease	23	6	3	1	3	0	0
19 - Coagulation factors inhibitors	1	1	1	0	0	1	0
20 - Myeloma - acute renal failure	56	10	1	0	5	5	0
21 - GVHD-Graft versus Host Disease	3306	235	103	35	121	37	16
22 - ABO-incompatible haematopoietic stem cell transplantation	85	33	13	8	11	0	1
23 - Transplantation-haematopoietic stem cells, anti-HLA antibodies	53	16	10	2	12	0	0
24 - Haemophagocytic syndromes	3	1	1	0	1	0	0
25 - Thrombocytopaenia / thrombosis induced by heparin	0	0	0	0	0	0	0
26 - Immunological thrombocytopaenias	0	0	0	0	0	0	0
27 - Hyperviscosity in hipergammaglobulinaemia	76	36	21	7	21	2	0
28 - Polycythaemia vera-Erythrocytosis	1858	838	164	8	446	19	5
29 - Post-transfusion purpura	0	0	0	0	0	0	0
30 - Red Cell Immunization, D-antigen-Prevention and treatment	0	0	0	0	0	0	0
31 - Anti-D immunization in pregnancy	52	4	1	1	0	0	0
32 - Acute Sickle Cell Disease	189	75	22	9	55	0	0
33 - Sickle Cell Disease, non-Acute Sickle Cell Disease	1653	267	18	91	137	5	0
34 - Thrombocytosis	8	6	4	0	6	0	0
35 - Thrombotic, coagulation-mediated microangiopathy	25	6	0	0	0	0	0
36 - Thrombotic, complement-mediated microangiopathy	25	9	7	0	2	5	2
37 - Thrombotic microangiopathy associated with drugs	2	1	0	0	0	1	0
38 - Thrombotic microangiopathy associated with infection	9	2	2	2	0	0	0
39 - Post-TMO thrombotic microangiopathy	62	5	0	0	4	0	1
40 - Thrombotic thrombocytopaenic purpura, TTP	1225	162	83	104	26	3	2
41 - Malaria	0	0	0	0	0	0	0
42 - Babesiosi	0	0	0	0	0	0	0
43 - Erythropoietic porphyria	11	3	0	0	0	1	0
44 - Hereditary haemochromatosis	167	71	34	0	71	0	0
992 - Other	301	104	5	1	100	0	2
Total	**9197**	**1895**	**494**	**269**	**1022**	**79**	**29**

Table 6
Neurological pathologies: number of procedures, number of treated patients, number of patients at first diagnosis and patients' outcome.

NEUROLOGY	Procedures (n)	Patients (n)	Patients at first diagnosis (n)	Patients' outcome			
				Remission	Improved	Unchanged	Worsened
1 - Acute disseminated encephalitis	233	44	28	1	17	14	2
2 - CIDP - Chronic inflammatory demyelinated polyneuropathy	1441	184	71	9	96	48	5
3 - Chronic focal Rasmussen encephalitis	10	2	0	0	0	1	1
4 - Guillain-Barré syndrome (GBS)	1303	255	161	46	117	27	8
5 - Complex regional pain syndrome	9	1	1	0	1	0	0
6 - Lambert-Eaton syndrome	109	10	4	0	5	0	1
7 - Multiple Sclerosis	257	40	9	1	26	11	0
8 - Myasthenia Gravis	2740	420	147	23	273	51	6
9 - Neuromyelitis optica	359	67	36	5	31	14	0
10 - NMDAR- antibodies encephalitis	112	21	12	2	13	3	0
11 - Paraneoplastic neurological syndromes	65	14	8	0	0	10	0
12 - Paraproteinemic demyelinating neuropathies	121	18	4	0	11	6	1
13 - PANDAS, Paediatric Neuropsychiatric Post-Streptococcal Syndrome	145	16	11	0	8	6	0
14 - Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	4	1	1	0	1	0	0
15 - VG-potassium channel (VGKC) antibody related Diseases	8	3	3	1	0	2	0
16 - Stiff person syndrome	54	10	3	2	5	3	0
991 - Other	280	49	28	0	17	26	1
Total	**7250**	**1155**	**527**	**90**	**621**	**222**	**25**

under discussion. In the ASFA 2023 Guidelines there are still numerous indications in category III, with a low grade of recommendation: the increase number of treated cases will help to confirm the results obtained so far.Among the kidney transplant recipients, 25 were ABO-incompatible and required 117 procedures. Recurrent heart rejection was the indication for 23 patients, who underwent 292 treatments. Prophylaxis of heart transplant rejection was performed in 12 patients, who underwent 161 treatments (13.4 treatments per patient). Desensitization for HLA or ABO antibodies involved patients scheduled for liver (16 procedures per 5 patients,), kidney (199 procedures per 44 patients). The overall outcome of the apheresis treatment is available for 195 patients (74 %): 117 out of 195 (60 %), showed a remission of the clinical picture (10.2 %) or its improvement (60 %).

Overall, as regards the 4 considered clinical specialties (Table 9), outcome data were available for 2656. Of these 83.4 % show a favorable response, consisting in the remission of the clinical picture or

Table 7
Rheumatological pathologies: number of procedures, number of treated patients, number of patients at first diagnosis and patients' outcome.

RHEUMATOLOGY	Procedures (n)	Patients (n)	Patients at first diagnosis (n)	Patients' outcome			
				Remission	Improved	Unchanged	Worsened
46 - ANCA-associated glomerulonephritis	117	21	14	2	11	2	2
48 - Cryoglobulinemia	225	28	15	4	11	3	1
49 - Schonlein-Henoch purpura	0	0	0	0	0	0	0
50 - Vasculitis	264	38	14	2	23	4	3
51 - Cardiac neonatal lupus	0	0	0	0	0	0	0
52 - Catastrophic Antiphospholipid-Acute Syndrome	50	11	3	2	4	0	0
53 - Scleroderma	61	11	5	3	4	4	0
54 - Systemic lupus erythematosus	48	8	3	0	4	1	1
994 - Other	99	17	5	1	5	6	1
Total	**864**	**134**	**59**	**14**	**62**	**20**	**8**

Table 8
Solid organ transplant: number of procedures, number of treated patients, number of patients at first diagnosis and patients' outcome.

SOLID ORGAN TRANSPLANT	Procedures (n)	Patients (n)	Patients at first diagnosis (n)	Patients' outcome			
				Remission	Improved	Unchanged	Worsened
77 - Heart Transplant-Recurrent Rejection	292	23	0	0	12	5	1
78 - Heart transplant - Prophylaxis of rejection	161	12	0	0	1	0	0
79 - Heart Transplant-Desensitization	0	0	0	0	0	0	0
80 - Heart Transplant-Ab-mediated Rejection	50	9	6	2	5	1	1
81 - Liver Transplant, ABO Desensitization (Living Donor)	0	0	0	0	0	0	0
82 - Liver transplant, ABO Desensitization (deceased donor)	1	1	1	0	1	0	0
83 - Liver transplant, Ab Rejection (ABO / HLA)	16	5	2	0	2	0	1
84 - Lung Transplant-BOS	574	65	6	0	29	29	3
85 - Lung Transplant-Ab-Mediated Rejection	167	23	4	0	6	4	0
86 - Lung Transplant-Desensitisation	0	0	0	0	0	0	0
87 - ABO compatible kidney transplant - Ab mediated rejection	401	76	27	5	39	6	1
88 - ABO compatible kidney transplant - Desensitization, living donor	44	9	9	7	2	0	0
89 - ABO compatible kidney transplant - Desensitization, deceased donor	38	10	4	0	5	3	2
90 - ABO Incompatible kidney transplant - Desensitization, living donor	117	25	18	6	12	0	0
91 - ABO Incompatible Kidney Transplant-Ab mediated Rejection	2	1	0	0	1	0	0
990 - Other	31	3	1	0	2	1	0
Total	**1894**	**262**	**78**	**20**	**117**	**49**	**9**

Table 9
Patients' outcome and number of assessable patients.

	Patients' outcome				
Specialty	**Assessable patients (n)**	**Remission**	**Improved**	**Unchanged**	**Worsened**
Haematology	1399	269	1022	79	29
Neurology	958	90	621	222	25
Solid organ transplant	195	20	117	49	9
Rheumatology	104	14	62	20	8
Total	**2656**	**393**	**1822**	**370**	**71**
% outcome	100.00	14.80	68.60	13.93	2.67

improvement respectively in 14.8 % and 68.6 % of the patients. Only 2.7 % of patients worsened, an effect attributed to the worsening of the disease.

As we reported previously, not all registered diseases fall within the coding provided by the ASFA guidelines. Both in the neurological field, which is the most numerous, and in other groupings of diseases, there are always some cases of patients whose disease is registered as "Other". Furthermore, the data highlight the use of therapeutic apheresis also in cases of autoimmune encephalitis, autoimmune cerebellitis with ataxia, myelitis. In the rheumatology field, in the "Other" category there are patients suffering from myositis/polymyositis, no longer present in the ASFA 2023 guidelines; in the hematological field, some cases of Waldenstrom's disease, cases of bone marrow aplasia and microangiopathy of unidentified origin fall into the "Other" category.

Finally, in Tables 10, 11 and 12 we report and compare the data regarding the number of procedures, the number of patients treated and the adverse events observed for the years 2019 to 2023, that is, since IRTA was included in the SISTRA. Table 10 indicates that there has been a progressive increase in apheresis procedures (from 23,657 in 2019 to 36,208 in 2023) with plasma exchange representing over 40 % of all procedures. In addition, despite SARS-CoV-2 infection has engaged all National Health Service, apheresis procedures increased from 23657 in 2019 to 33681 in 2021. As can be seen in Table 11, patients treated with therapeutic apheresis also increased from 5253 in 2019 to 8596 in 2023. Patients treated with plasma exchange and stem cell collection represent over 50 % of the total patients. Table 12 shows a reversal of the trend in adverse effects: despite the increase in apheresis procedures and patients treated, adverse effects of any kind are clearly decreasing. Regarding the

Table 10
Therapeutic apheresis procedures for the years 2019 to 2023.

	N. Procedures				
	2019	**2020**	**2021**	**2022**	**2023**
Therapeutic procedure					
1 - Plasma exchange	11458	11272	12562	13485	15064
2 - Cascade filtration	484	600	797	569	596
3 - Plasma adsorption (physical, chemical)	0	0	240	70	109
4 - IgG / IgE Immunoadsorption	235	138	192	43	39
5 - Photopheresis (online)	1624	2774	3012	3532	4525
6 - Photopheresis (off line)	2921	4776	6052	5635	4695
7 - Lipoprotein apheresis	377	441	657	584	670
8 - Lymphoplasmapheresis	16	0	7	0	2
9 - Cytoreductive leukapheresis	199	75	98	75	64
10 - Granulocyte-monocyto-apheresis	342	255	294	242	195
11 - Therapeutic platelet apheresis	12	30	36	21	40
12 - Erythrocyte exchange	1274	2110	2203	2389	2652
13 - Erythro-apheresis	2457	2787	3300	3418	2885
14 - Stem Cell Collection (autotransplant)	2192	3236	3548	4212	4135
15 - Other:	66	56	683	427	537
Total	**23657**	**28550**	**33681**	**34702**	**36208**

Table 11
Number of patients treated, including paediatric patients for the years 2019 to 2023.

	N. Patients (Including paediatric patients)				
	2019	**2020**	**2021**	**2022**	**2023**
Therapeutic procedure					
1 - Plasma exchange	1942	1871	2103	2357	2277
2 - Cascade filtration	78	77	108	93	89
3 - Plasma adsorption (physical, chemical)	0	0	7	7	13
4 - IgG / IgE Immunoadsorption	20	18	22	7	5
5 - Photopheresis (online)	84	147	184	214	292
6 - Photopheresis (off line)	235	475	689	735	739
7 - Lipoprotein apheresis	38	42	58	45	28
8 - Lymphoplasmapheresis	7	0	5	0	2
9 - Cytoreductive leukapheresis	170	43	63	39	39
10 - Granulocyte-monocyto-apheresis	48	33	42	33	27
11 - Therapeutic platelet apheresis	9	11	19	17	19
12 - Erythrocyte exchange	231	366	534	454	520
13 - Erythro-apheresis	827	988	1099	1530	1343
14 - Stem Cell Collection (autotransplant)	1546	2197	2455	2922	2817
15 - Other:	18	53	496	328	386
Total	**5253**	**6321**	**7884**	**8781**	**8596**

Table 12
Total adverse events to Therapeutic Procedures for the years 2019 to 2023.

	2019	**2020**	**2021**	**2022**	**2023**
Mild	1027	975	967	791	841
Moderate	76	198	107	99	40
Severe	17	8	9	4	9

adverse effects of therapeutic apheresis procedures and the number of patients treated, no substantial differences were recorded between the years 2022 and 2023.

4. Discussion

The present report from the IRTA registry is an update on the collected data from apheresis centers within the Italian transfusion system for different indications and techniques and referred to the 2023 activity data. We have observed an increase in apheresis procedures which went from 34702 performed in 2022 to 36208 in 2023 (+4.3 %) confirming the positive trend recorded from 2019 onwards [4–6]. Regarding the adverse effects of therapeutic apheresis procedures, the data from this study confirm that therapeutic apheresis is a safe procedure with an extremely limited number of adverse events, especially severe ones [6]. Adverse effects were reported primarily for therapeutic plasma exchange and peripheral stem cell collection procedures with a frequency that resulted essentially unchanged compared to 2022 [890 in 2023 (2.6 %) vs 894 in 2022 (2.5 %)], but clearly decreased with respect to previous years (2019–2021): in almost all cases these are mild adverse events attributable to hypocalcemia. Furthermore, outcome data from IRTA registry show that therapeutic apheresis is associated with a general improvement of clinical conditions. Among the most recent studies on the topic, the World Apheresis Association (WAA) reports activity data for the period 2018–2022 [7]: 9500 patients were treated with 58355 apheresis procedures; most patients underwent cytoapheresis, while the most used procedure is plasma-exchange, similarly to what has been observed for some years in Italy. Regarding adverse events, the WAA reports the incompleteness of data entry, similarly to what has been observed in Italy. Regarding the severity of adverse events, moderate severity events clearly prevail, but the list of events and the related severity score is not available. On the contrary, in the IRTA, most events have always been mild.

As regards the "Other" category, the neurological field is of particular interest. In this category, pathologies have been recorded for which the use of therapeutic apheresis is not yet supported by literature evidence, but for which there is a rational immunological basis that justifies the use of apheresis. These pathologies are not foreseen in the ASFA Guidelines; however, in this type of situation, regardless of the guidelines, the McLeod principles (rationale-based criteria for use of TA) [8] must always apply. When these principles are respected, apheresis treatment is justified. On the other hand, the diseases in which therapeutic apheresis can be indicated are all rare diseases, and it is often very difficult to reach a sufficient number of cases to carry out a randomized and controlled clinical trial, as foreseen by the guidelines. The IRTA Registry allows collecting reports of similar clinical cases, sharing experiences and providing useful information to improve apheresis care.

It is also worth mentioning the start of lymphocyte collection for the preparation of Car-T: in light of this, a specific entry should be considered in the next edition of the National Register of Therapeutic Apheresis.

In conclusion, we believe that the IRTA represents a strategic resource for the National Health Service, the regional health authorities and the scientific community and that collecting and analyzing information on therapeutic apheresis procedures and patient outcomes will help to improve apheresis care and outcomes in the future.

CRediT authorship contribution statement

Vanessa Piccinini: Data curation. **Simonetta Pupella:** Supervision. **Liviana Catalano:** Writing – original draft, Software, Methodology, Conceptualization. **Giuseppe Marano:** Writing – original draft, Software, Methodology, Conceptualization. **Angelo Ostuni:** Supervision. **Vincenzo de Angelis:** Supervision. **Giustina De Silvestro:** Writing – original draft, Software, Methodology, Conceptualization.

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