

Results of ART treatments **as of 2023** **S.I.S.Me.R. – Bologna and Satellite Centers**

TABLE 1 - Cumulative data S.I.S.Me.R.'s Centers

Years of activity	1985-1996	1997-1998	1999-2003	2004-2008	2009-2012	2013-2015	2016-2018	2019-2021	2022	2023
No. of initiated cycles	4553	1158	4351	3580	3112	1731	1221	886	252	207
Maternal age (mean±SD)	34.3±5	35.1±5	35.4±6	37.2±5	37.4±6	37.5±7	37.2±4.8	37.8±4.6	37.9±4.4	37.4±4.5
Maximum number of embryos transferred	4-5	2-3	2	3	2 - (3)	1-2	2	2	2	1
No. of embryo transfers	2616	715	2530	2439	2039	999	510	297	55	30
Pregnancy rate per transfer	20%	37%	32%	25.8%	26.1%	28%	17.3%	25.3%	25.5%	10%
Implantation rate	9%	23%	21%	16%	16%	16%	12.4%	17.6%	19.6%	10%
Miscarriage rate	25%	11%	15%	18%	18%	20%	13.6%	22.7%	28.6%	33.3%

TABLE 2 - IVF – ICSI S.I.S.Me.R. Centers (1997 – 2023)

	IVF (fresh cycles)	ICSI (Fresh cycles)	Surgical ICSI
No. of initiated cycles	3986	11576	928
No. of cancelled cycles	857	2162	98
No. of oocyte retrievals	3129	9414	830
No. of embryo transfers	2363	6686	563
No. of clinical pregnancies/transfer (%)	77 (32.9%)	1770 (26.5%)	141 (25%)
No. of miscarriages	83	316	8
No. of ectopic pregnancies	17	49	1

Through the years, Assisted Reproduction techniques quickly evolved.

The number of IVF cycles progressively decreased, while that of ICSI cycles has been constantly growing.

At S.I.S.Me.R. this is mostly due to the increase of PGT cycles (for which ICSI is required) and of cases of severe male factor of infertility.

In other Centers, ICSI is used indiscriminately for all patients, but this does not improve outcomes in the absence of specific indications.

TABLE 3 - Age factor S.I.S.Me.R. Centers (2002 – 2023)

Age (Years)	<29 yrs	30-34 yrs	35-37 yrs	38-40 yrs	41-43 yrs	>44 yrs
No. of initiated cycles	818	3074	2768	2703	1907	948
No. of cancelled cycles	98	380	467	451	401	362
% of cancelled cycles	12%	12.4%	16.9%	16.7%	21.0%	38.5%
No. of oocyte retrievals	720	2694	2301	2252	1506	583
No. of collected oocytes (mean±SD)	9.0±5.1	8.4±4.7	7.4±4.5	7.1± 4.6	6.3±4.7	4.6± 3.1
No. of embryo transfers	510	1991	1701	1600	1083	318
No. of clinical pregnancies	199	686	525	369	150	14
Pregnancy rate	39.0%	34.5%	30.9%	23.1%	13.9%	4.4%
No. of miscarriages	20	70	66	83	61	5
Miscarriage rate	10.1%	10.2%	12.6%	22.5%	40.7%	35.7%
No. of ectopic pregnancies	6	18	16	14	4	0
Implantation rate	26,3%	22.0%	19.0%	12.9%	6.7%	2.2%

TABLE 4 – Transfer of cryopreserved embryos/ zygotes/ oocytes

	EMBRYOS 1985-1995	EMBRYOS/ZYGOTES 1996-2023	BLASTOCYSTS 2010-2023	OOCYTES 2004-2023
No. of thawing cycles	302	2858	1808	1051
No. of embryo transfers	228	2455	1739	841
No. of clinical pregnancies	17 (7.5%)	658 (26.8%)	602 (34.6%)	144 (17.1%)
No of miscarriages	8	142	132	38
No. of ectopic pregnancies	0	7	12	5

In 2009 the Italian Constitutional Court abolished the obligation to generate max. 3 embryos to be transferred simultaneously and the ban on cryopreservation. Since then, clinicians have been allowed to resort to embryo cryopreservation whenever required.

Advantages of this technique include:

- Possibility to repeat treatments more easily without having to undergo ovarian stimulation and oocyte retrieval every time (with all related costs, risks and discomfort)
- Reduced risk of OHSS (Ovarian Hyper Stimulation Syndrome)
- Possibility to perform preimplantation genetic testing (PGT) on embryos
- Possibility to perform an optimal endometrial preparation

Outcomes of frozen embryo transfers are comparable to those of fresh embryo transfers.

TABLE 5 – Transfer of vitrified oocytes and blastocysts

	Vitrification	
	Oocytes 2004-2023	Blastocysts 2010 - 2023
No. of thawing cycles	195	1787
No. survived/ thawing	834/1157 (72.1%)	1893/2230 (84.9%)
No. of embryo transfers	133	1724
No. of clinical pregnancies	36/133 (27.1%)	598/1724 (34.7%)
No. of miscarriages	11	131
No. of ectopic pregnancies	1	12

TABLE 6 - Transfer of zygotes/oocytes/blastocysts following cryopreservation for ovarian hyperstimulation (OHSS) risk

	1996-2015 (zygotes)	2004-2014 (oocytes)	2010-2023 (blastocysts)
No. of cryopreservation cycles for OHSS risk	731	224	348
No. of thawing cycles	1271	338	588
No. of patients who performed at least 1 thawing cycle	699	209	324
No. of embryo transfers	1151	294	577
No. of clinical pregnancies	367	56	216
Pregnancy rate per transfer	(32 %)	(19 %)	(37.4 %)
Pregnancy rate per patient	(53 %)	(27 %)	(66.7 %)
No. of miscarriages	72	15	45
No. of ectopic pregnancies	0	0	3

TABLE 7 - Social freezing 2015-2023

No. of patient undergoing treatment (mean age \pm SD)	22 (36.6 \pm 6.9)
No. of initiated cycles	25
No. of cancelled cycles	2
No. of oocyte retrievals	23
Mean number of collected oocytes \pm SD	8.7 \pm 5.5
Mean number of vitrified oocytes \pm SD	7.7 \pm 5.5
No. of patients who used their cryopreserved oocytes for an assisted reproduction treatment	0
No. of patients who donated their oocytes for scientific research purposes	1

In the last few years, the number of women who decide to cryopreserve their oocytes to postpone motherhood with better chances of success has been constantly increasing.

As of today, the usage rate of cryopreserved oocytes is limited, since the majority of treatments have been performed in the last 2-3 years.

TABLE 8 - IVF Lite Programme – Results (Cumulative data 2008-2023)

No. of couples admitted in the programme	592
Mean maternal age \pm SD	33.5 \pm 3.1
No. of couples excluded from the program due to inadequate ovarian response	147
No. of couples who completed the programme	423
No. of oocyte retrievals	692
Mean number of collected oocyte per oocyte retrieval \pm SD	6.1 \pm 2.8
No. of embryo transfers (fresh or frozen embryos)	886
No. of full term pregnancies	271/423 (64.1% per patient)

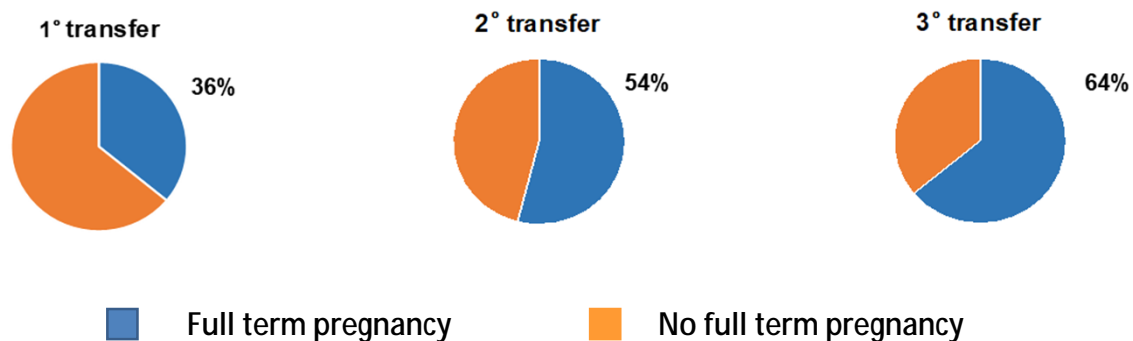


TABLE 9 - I level treatments (intrauterine insemination or IUI)

	Own gametes (2001 – 2023)	Donor sperm (2016 – 2023)
No. of couples	571	55
Mean maternal age	36.2	33.9
No. of cycles	1210	102
No. of clinical pregnancies	101	13
Pregnancy rate per cycle	8.3%	12.7%
Pregnancy rate per couple	17.7%	23.6%
No. of miscarriages	23	2
No. of ectopic pregnancies	6	0

TABLE 9B - Donor sperm treatments

	I level (IUI) 2016-2023	II level (IVF/ICSI) 2016-2023
No. of couples	55	64
Mean maternal age	33,9	35,5
No. of. Cycles	102	76
No. of clinical pregnancies	13	34
Pregnancy rate per cycle	12,7%	44,7%
Pregnancy rate per couple	23,6%	53,1%
No. of miscarriages	2	5
No. of ectopic pregnancies	0	0

TABLE 10 - Oocyte donation programme (2015-2023)

Donor oocyte thawing cycles	438
No of fresh embryo transfer deriving from thawed donor oocytes	408
No. of clinical pregnancies	154
Pregnancy rate per transfer	37.7 %
Miscarriages + ectopic pregnancies	18+4 (14.3%)
No of patients with cryopreserved surplus embryos	310
No. of frozen embryo transfers	256
No. of clinical pregnancies	71
Pregnancy rate per transfer	27,7 %
Miscarriages + ectopic pregnancies	17 (23.9 %)

INTRODUCTION TO TABLES 11, 11B e 11C - Embryo banking for Preimplantation Genetic Testing PGT-M, PGT-SR e PGT-A

PGT requires sophisticated technology, specialized staff and a dedicated organization, therefore it is indicated only for couples at high reproductive risk.

In order to maximize efficacy and effectiveness of this technique, limiting costs while ensuring reasonable chances of a successful outcome it is necessary that a suitable number of embryos is available for analysis.

However, it is not always possible to obtain a suitable number of embryos with a single oocyte retrieval. For this reason, patients can enter an embryo banking programme. This programme implies performing several oocyte retrievals cryopreserving embryos obtained until the suitable number for analysis is achieved.

In view of the above, in the following tables the number of oocyte retrievals and that of analysis performed will be indicated separately. The number of analysis is lower than the number of oocyte retrievals, because in case of embryo banking one analysis can include embryos deriving from multiple oocyte retrievals.

TABLE 11B - Treatments with Preimplantation Genetic Testing for Monogenic diseases PGT-M (1997 -2023)

No. of patients	135
No. of oocyte retrievals	241
No. of PGT-M analysis	169
Mean maternal age \pm SD	34.9 \pm 3.5
No. of oocytes retrieved (Mean \pm SD)	2359 (9.8 \pm 4.8)
No. of analyzed blastocysts	974
No. of diagnosed blastocyst/analyzed blastocysts (%)	883/974 (90.7%)
No. of transferrable blastocysts (nomal + carrier)/ analyzed blastocysts (%)	539 /974 (55.3%)
No. of non-transferrable blastocysts/analyzed blastocysts (%)	344/974 (35.3%)
No. of transferred blastocysts	223
No. of clinical pregnancies	82
Pregnancy rate per transfer	36.8%
Miscarriages + ectopic pregnancies	18

The following slide includes a list of pathologies for which PGT-M was performed at S.I.S.Me.R.

Pathology	Patients	Pathology	Patients
Aicardi Goutieres syndrome	1	Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS)	1
Alpha-thalassemia x-linked intellectual disability (ATRX)	1	Mucopolysaccharidosis	1
Citrullinemia	1	Myotonic dystrophy	12
Combined oxidative phosphorylation deficiency 12 (COXPD12)	1	Neurofibromatosis type 1 (NF1)	2
Cystic Fibrosis	34	Optic Atrophy	1
Duchenne muscular dystrophy (DMD)	4	Osteogenesis imperfecta type 1	1
Epidermolysis bullosa	2	Paramyotonia congenita	2
Familial Adenomatous Polyposis	1	Polycystic kidney disease	3
Fascioscapulohumeral dystrophy (FSHD)	1	Pompe syndrome	1
Fragile X syndrome	4	Primary dystonia	1
Glucose 6 phosphate dehydrogenase (G6PD) deficiency	1	Retinitis pigmentosa	2
Haemophilia A	7	Simpson-Golabi-Behmel syndrome	1
Holt-Oram syndrome	1	Spastic paraparesis	1
Huntington Chorea	9	Spinal Muscular Atrophy (SMA)	2
Kennedy Disease	2	Thalassemia	25
Leigh syndrome	1	Thomsen disease	1
Lesch Nyhan syndrome	1	Tuberous Sclerosis	1
Marfan syndrome	1	Von Hippel-Lindau	1
Merosin-deficient congenital muscular dystrophy	1	X-Linked Severe Combined Immunodeficiency (SCID-X1)	1
Methylmalonic aciduria	1		

TABLE 11B - Treatments with Preimplantation Genetic Testing for Structural Rearrangements PGT-SR (2009 – 2023)

	Robertsonian Translocations	Reciprocal Translocations	Deletions	Inversions	Duplications
No. of patients	34	54	2	3	1
No. of oocyte retrievals	55	89	5	4	4
No. of PGT-SR analysis performed	46	68	4	4	1
Mean maternal age \pm SD	35.1 \pm 2.4	35.9 \pm 4.7	37.1 \pm 3	37.2 \pm 2.2	36.5
No. of oocytes retrieved (Mean \pm SD)	544 (10.2 \pm 4)	849 (9.5 \pm 3.8)	72 (14 \pm 2.8)	35 (8.8 \pm 3.9)	45 (11.2)
No. of analyzed blastocysts	419	607	28	18	9
No. of transferrable blastocysts (normal/balanced + euploid)/analyzed blastocysts (%)	104 (24.8)	98 (16.1)	5 (17.8)	5 (27.7)	1 (11.1)
No. of transfers	39	42	3	5	1
No. of clinical pregnancies	17	10	1	3	0
Pregnancy rate per transfer	43.6%	23.8%	25%	60%	0
Miscarriages + ectopic pregnancies	5	2	0	0	0

TABLE 11C - Treatments with Preimplantation Genetic Testing for Aneuploidies PGT-A

	TROPHECTODERM BIOPSY 2009 - 2023
No. of patients	318
No. of oocyte retrievals	463
No. of PGT-A analysis performed	251
Mean maternal age \pm SD	389 \pm 3.8
No. of collected oocytes (Mean \pm SD)	4301 (9.2 \pm 2.7)
No. of analyzed blastocysts	1217
No. of diagnosed blastocysts/analyzed blastocysts (%)	1167 (95.9)
No. of transferrable blastocysts/analyzed blastocysts (%)	460 (39.4)
No. of transfers	265
No. of clinical pregnancies	120
Pregnancy rate per transfer	45,3
Miscarriages + ectopic pregnancies	26

TABLE 12 - Cumulative data per technique

	IVF	ICSI	MESA/ TESE	Cryopreserved zygotes embryos	Cryopreserved oocytes	Cryopreserved blastocysts	PB 1 Biopsy	PB 1 + PB 2 Biopsy	Embryo biopsy	PBs + embryo biopsy	Oocyte donation	GIFT/ TET	IUI
No. of cycles	5635	9870	951	3108	1057	1691	1191	313	2060	138	1527	628	1279
No. of oocyte retrievals	4384	8025	865	-	-	-	1076	298	1763	116	-	525	-
No. of transfers	3605	5897	592	2683	843	1631	933	192	986	43	1398	510	-
No. of clinical pregnancies	1012	1511	132	675	144	565	188	29	299	12	340	162	113
No. of miscarriages	170	275	12	150	38	118	42	6	52	2	68	31	22
No. of ectopic pregnancies	19	40	1	10	5	11	7	1	8	0	5	4	6
No. of heterotopic pregnancies	3	1	0	0	0	0	0	0	0	0	1	0	0
No. of therapeutic abortion + stillbirths	6	14	2	5	0	1	4	0	2	1	3	0	0

TABLE 13- Pregnancies and babies (Transfers 1985 - 2022)

Clinical pregnancies	4973
Lost to follow up	48
Miscarriages	988 (19.8 %)
Ectopic pregnancies	102 (2 %)
Prenatal diagnosis (including NIPT)	1340 (32 %)
Therapeutic abortions + stillbirths	42 (0.8 %)
Deliveries	3775
Single	3102 (82.1 %)
Twins	606 (16.0 %)
Triplets	64 (1.6 %)
Quadruplets	3 (0.07 %)
Babies born	4518
No. of malformations reported	160 (4 %)
Babies born with malformations	116 (2.9 %)