Science is a way of thinking much more than it is a body of knowledge.
Carl Sagan

International Winter School

Genome integrity and genome organization in physiology and pathology

December 18-22 2023

Preliminary program

December 18th
10-10.30 Opening and registration

Nuclear Integrity and chromatin organization
Discussant: Romina Burla, IBPM-CNR Rome

10.30-11.45 **Wenting Zhao**, *NTU Singapore* (online)
Engineered membrane deformation and guided reorganization of cellular machinery to study mechanical properties of cells

11.45-13.00 **Fred Bernard**, *Jacques Monod Institute, Paris, France*
The importance of nucleus positioning in embryos development

14.00-15.30 **Jeremy Carlton**, *King's College (anch*e GBM students)
The ESCRT machinery at nuclear envelope: Closing holes and expanding roles

15.30-17.00 ***Barbara Peruzzi*** *(IRCCS Children Hospital Bambino Gesù Italy)*
Nuclear lamins and nuclear dysmorphism in pathologies through advanced microscopy lens

December 19th
Chromatin organization in development
Discussant: Chiara Mozzetta, IBPM-CNR Rome

10.00-11.30 ***Philippe Collas*** *(University of Oslo*)
title tbd

11.30-13.00 ***Fulvio Chiacchiera*** *(University of Trento)*

14.00-15.30 ***Daniela Palacios*** *(Cattolica Huniversity of Rome)*

15.30-17.00 **tbd**

December 20th

Genome Stability in mouse model of diseases

Discussant: Eleonora Centofante, Sapienza University of Rome

10.00-11.30 ***Jamie Hackett**, European Molecular Biology Laboratory (EMBL Monterotondo)*
What do chromatin modifications do? Epigenome editing to dissect function in health and disease?

11.30-13.00 ***Monica Ballarino** (Sapienza, University of Rome)*
Myogenesis and long non-coding RNAs: a chromatin affair

14.00-15.30 ***Marina Vietri** (University of Oslo, Norway)*
Nuclear envelope dynamics at ruptured micronuclei

15.30-17.00 ***Rafal Czapiewski** (University of Edinburgh, UK) online*
Nuclear envelope controls genetic spacetime - focus on genome organization and function.

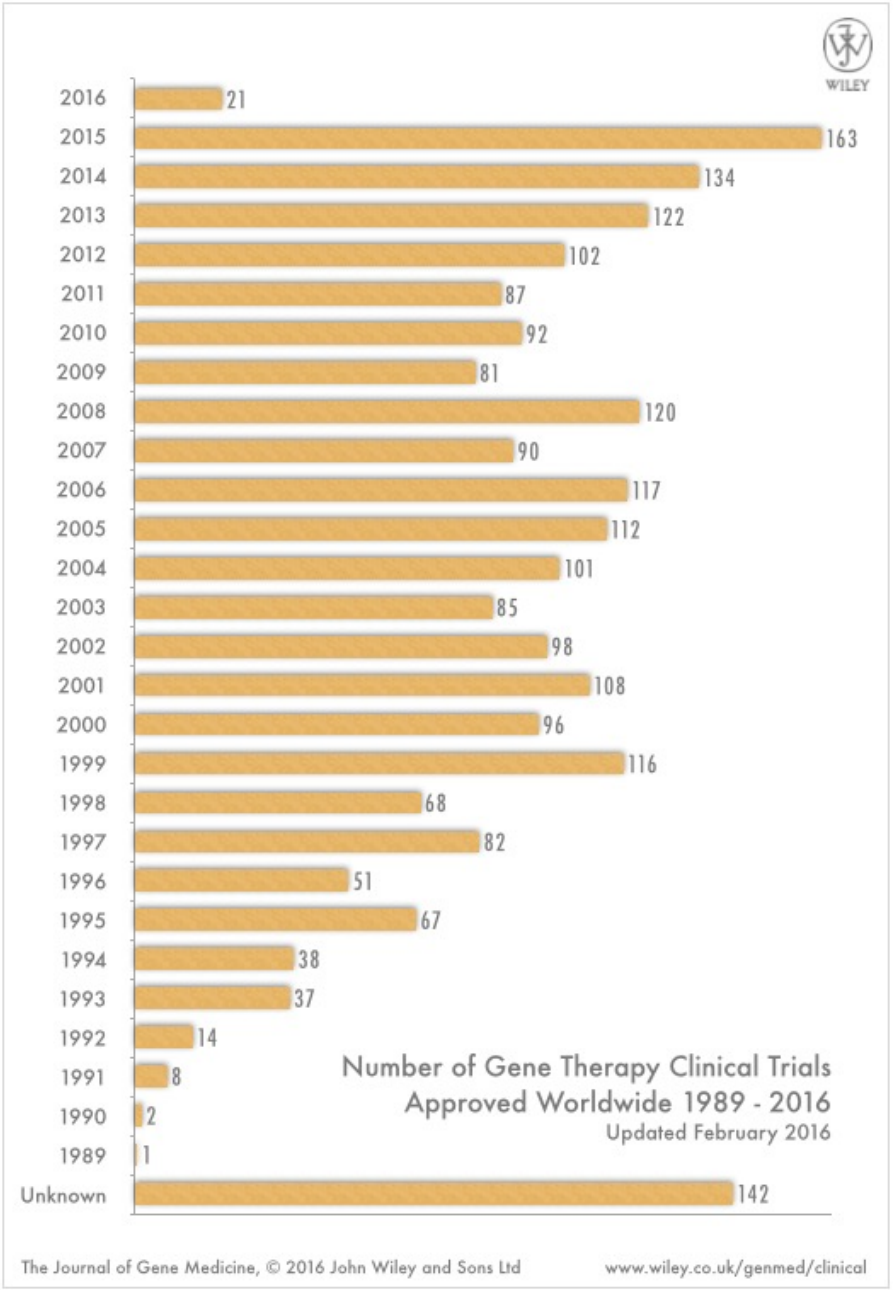
December 21th

10.00-13.00 **International Poster Session**

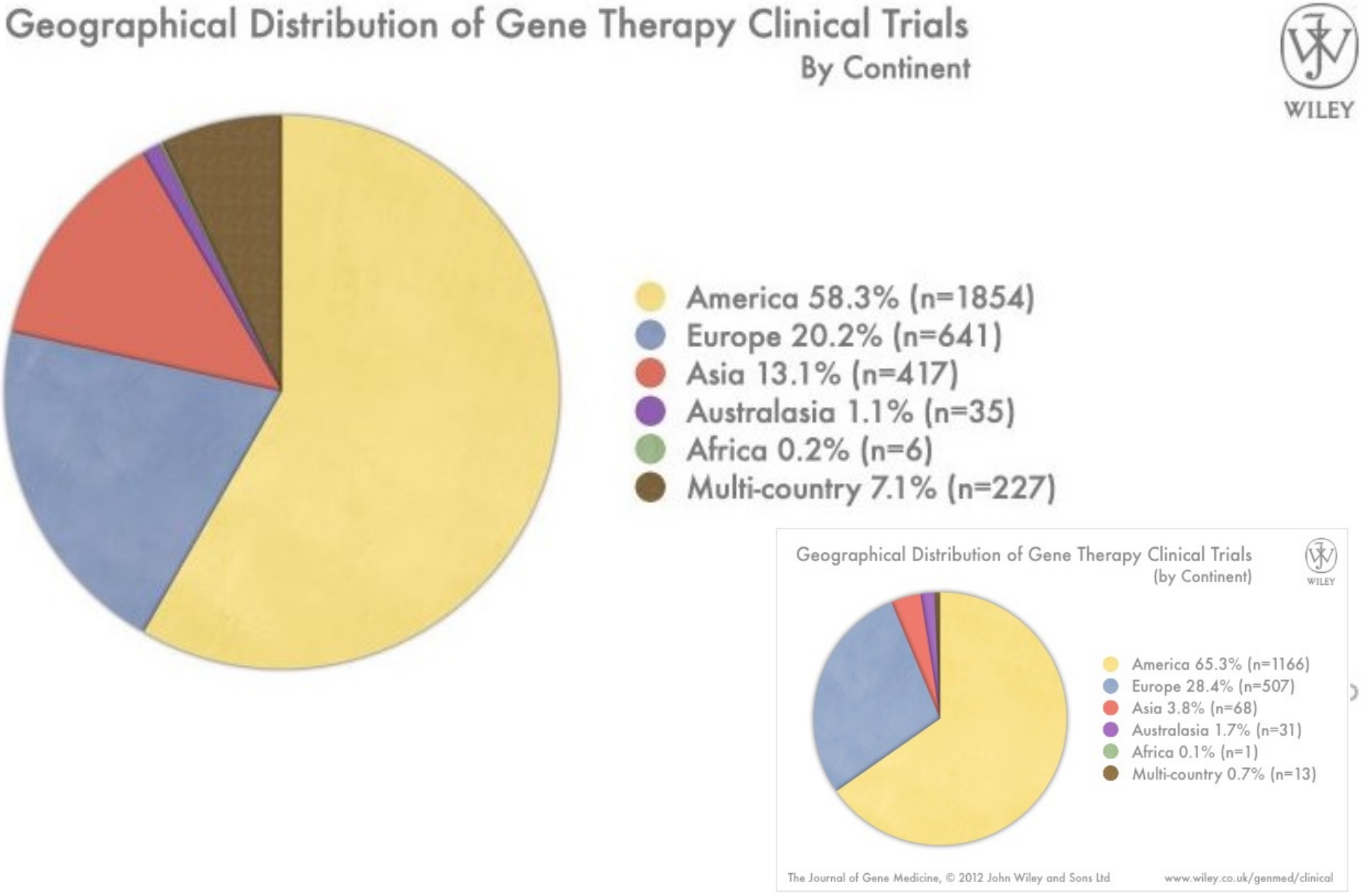
14.00-17.00 **Italian Poster Session**

17.30 **Best poster awards**

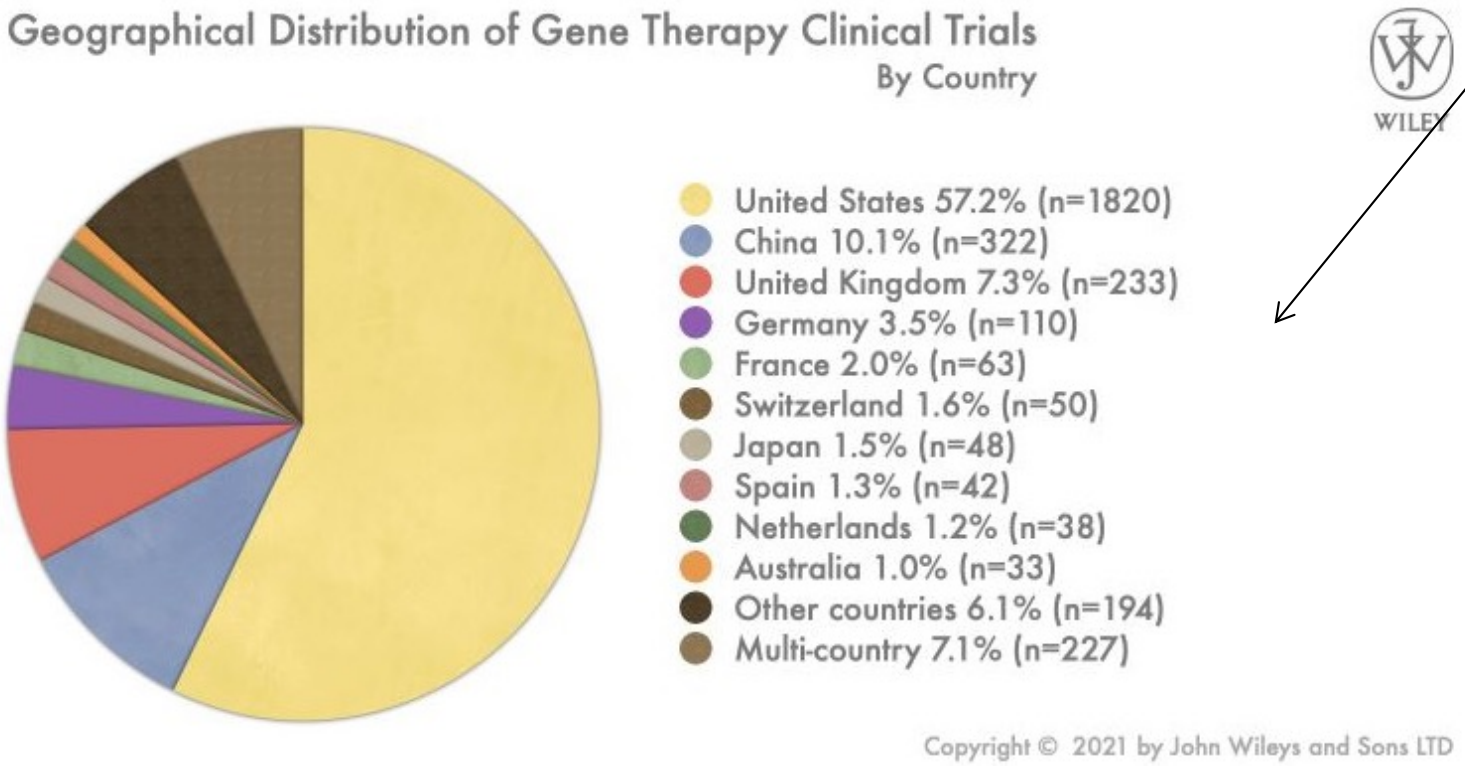
Clinical trials – 2016 update



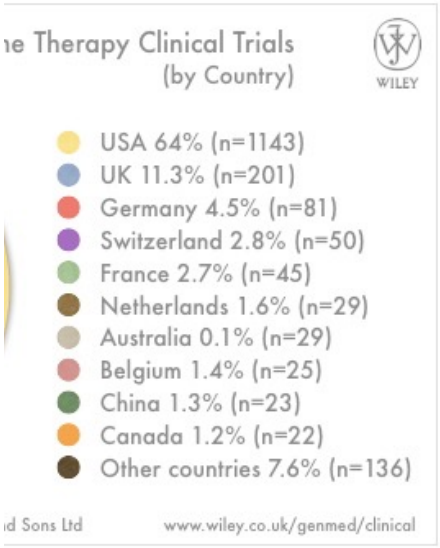
Trials/continent



Trials/country

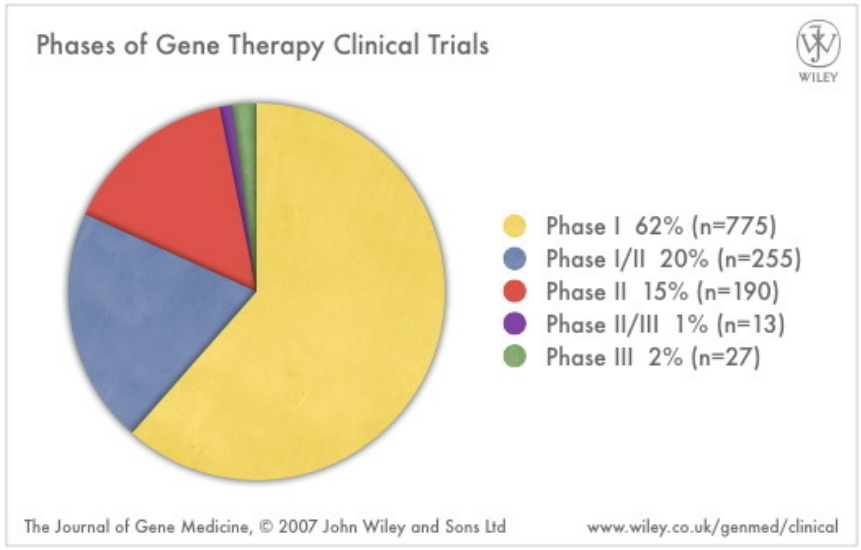


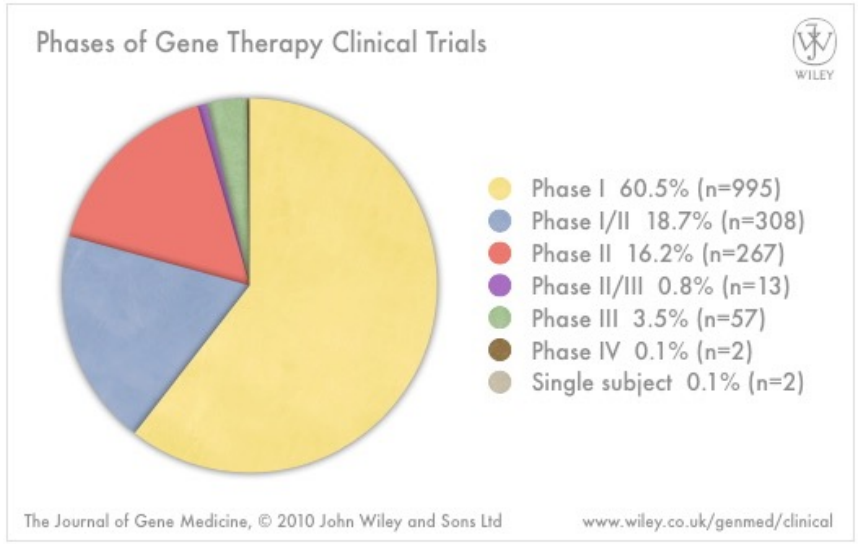
in 2012

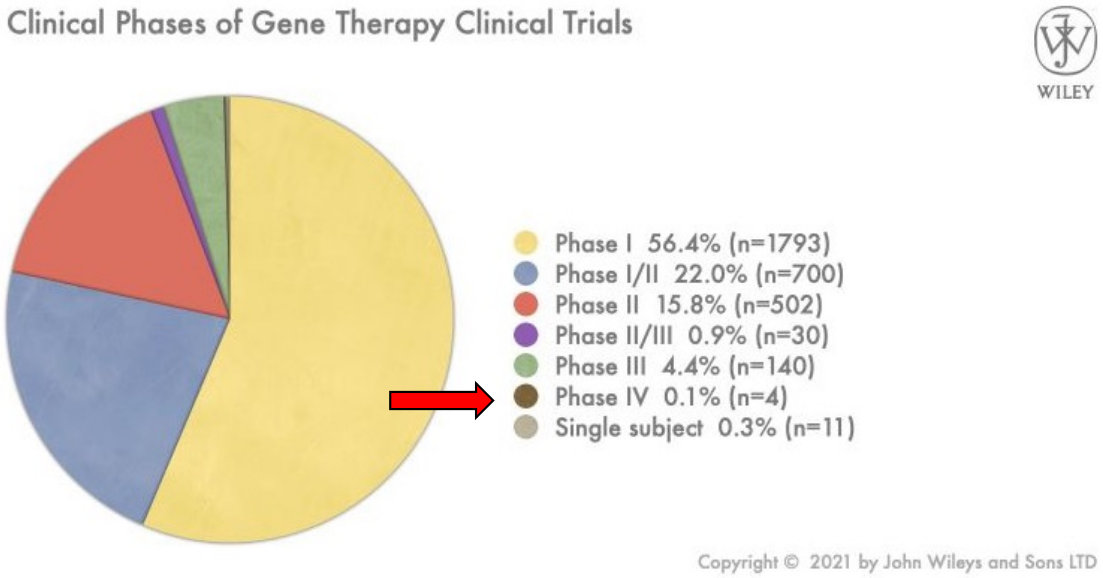


Country	Gene Therapy Clinical Trials	
	Number	%
Italy	36	1.1%
France	63	2.0%

Gene therapy trial phases







Which are the trial phases

- Phase I: small number of patients (20-80) for pharmacovigilance, pharmacokinetics, pharmacodynamics

- Phase II: performed on larger groups (20-300) and designed to assess clinical efficacy of the therapy; as well as to continue Phase I assessments

- Phase III: randomized controlled trials on large patient groups (300-3000 or more depending upon the condition) and are aimed at being the definitive assessment of the efficacy of the new therapy, in comparison with current 'Gold Standard' treatment.

- Phase IV: involve the post-launch safety surveillance and ongoing technical support of a drug.

Approved gene therapy products

Approved gene therapy products.

Year of Approval	Trade name (General name)	Manufacturer	Vector	Transferred gene/ genetic modification	Indication	*Ex-vivo/in-vivo* (target cell)	Approving country/Agency	Details
1998	Vitravene (Fomivirsen) [64]	Isis Pharmaceuticals	RNA	Antisense oligonucleotide against *UL123* gene of CMV	Local treatment of cytomegalovirus retinitis in immunocompromised patients	*In-vivo*	FDA/ EMA	First approved gene therapy drug, later withdrawn from the market in 2002
2003	Gendicine (rAd-p53) [65,66]	Shenzhen SiBiono GeneTech	Adenovirus	*P53*	Head and neck cancer	*In-vivo*	SFDA	First commercial gene therapy drug
2005	Oncorine (H101) [18]	Shanghai Sunway Biotech	Adenovirus	*E1B*-deleted adenovirus	Nasopharyngeal carcinoma	*In-vivo*	SFDA	First oncolytic virus product
2007	Rexin-G (Mx-dnG1/ DeltaRex-G) [67]	Epeius Biotechnologies	Retrovirus	Mutant form of the cyclin G1	Soft tissue sarcoma and osteosarcoma	*In-vivo*	Philippines	
2011	Neovasculgen (Cambiogenplasmid/ PI-VEGF165) [68]	Human Stem Cells Institute	Plasmid	VEGF	Peripheral vascular disease and limb ischemia	*In-vivo*	Russian Ministry of Healthcare, Ukraine	First plasmid-based medicine
2012	Glybera (alipogene tiparvovec) [69]	UniQure	AAV1	lipoprotein lipase (*LPL S447X*)	Familial lipoprotein lipase deficiency	*In-vivo*	EMA	First gene therapy product in the European Union, later withdrawn from the market in 2017
2013	Kynamro (Mipomersen) [64]	Ionis Pharmaceuticals	RNA	Antisense oligonucleotide against *ApoB100*	Homozygous familial hypercholesterolemia	*In-vivo*	FDA, Mexico, Argentina, South Korea	Later withdrawn in 2019 by FDA
2015	Imlygic (Talimogene Laherparevec)[70,71]	Amgen	HSV1	Addition of GM-CSF, deletion of ICP47 and ICP34.5	Melanoma	*In-vivo*	FDA, EMA, UK, Australia	Oncolytic virus product

Approved gene therapy products

2016	Zalmoxis [72]	MolMed	Retrovirus	ΔLNGFR and HSV-TK Mut2	Restoring the immune system of the patient after hematopoietic stem cell transplantation	*Ex-vivo* (T cell)	EMA	Genetically modified allogeneic T cell, later withdrawn in 2019 in Germany
2016	Strimvelis (GSK2696273) [73–76]	Orchard Therapeutics	Retrovirus	Adenosine deaminase (*ADA*)	Severe combined immunodeficiency (SCID) due to ADA deficiency	*Ex-vivo* (CD34 + cell)	EMA, UK	First corrective *ex-vivo* stem cell (autologous CD34 + cells) gene therapy in the world
2016	Exondys 51 (Eteplirsen) [77,78]	Sarepta Therapeutics	RNA	Antisense oligonucleotide for *dystrophin*	Duchenne Muscular Dystrophy (DMD)	*In-vivo*	FDA	
2016	Spinraza (Nusinersen) [77,79]	Ionis Pharmaceuticals	RNA	Antisense oligonucleotide for *SMN2*	Spinal Muscular Atrophy	*In-vivo*	FDA, EMA, UK, Canada, Japan, Brazil, Switzerland, Australia, South Korea, SFDA, Argentina, Colombia, Taiwan, Turkey	
2016	Ampligen (Rintatolimod/ Poly (C12U)) [80]	AIM ImmunoTech	RNA	Antisense double stranded RNA oligonucleotide as a TLR3 agonist	Chronic fatigue syndrome/ myalgic encephalomyelitis	*In-vivo*	Argentina, FDA (Compassionate use)	
2017	Kymriah (Tisagenlecleucel) [81]	Novartis	Lentivirus	*CD19* CAR	Relapsed B cell acute lymphoblastic leukemia	*Ex-vivo* (T cell)	FDA, EMA, UK, Japan, Australia, Canada, South Korea	First CAR T cell using lentivirus
2017	Luxturna (Voretigene Neparvovec-rzyl) [82]	Spark Therapeutics (Roche)	AAV2	*RPE65*	RPE65 mutation-associated retinal dystrophy	*In-vivo*	FDA, EMA, UK, Australia, Canada, South Korea	First FDA-approved *In-vivo* AAV gene

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Approved gene therapy products

Table 1 (*continued*)

Year of Approval	Trade name (General name)	Manufacturer	Vector	Transferred gene/ genetic modification	Indication	*Ex-vivo/in-vivo* (target cell)	Approving country/Agency	Details
								therapy product
2017	Yescarta (Axicabtagene Ciloleucel) [83]	Kite Pharma (Gilead)	Retrovirus	*CD19* CAR	Relapsed or Refractory large B cell lymphoma	*Ex-vivo* (T cell)	FDA, EMA, UK, Japan, Canada, SFDA	First CAR T cell using retrovirus
2017	Invossa (chondrocytes transduced with TGF-ß1) [84,85]	Kolon TissueGene	Retrovirus	TGF-β1	Moderate Knee Arthritis	*Ex-vivo* (chondrocyte)	Korea	First gene therapy product in Korea
2018	Tegsedi (Inotersen) [86]	Ionis Pharmaceuticals	RNA	Antisense oligonucleotide against transthyretin mRNA	Hereditary Transthyretin-related Amyloidosis	*In-vivo*	EMA, UK, Canada, FDA, Brazil	
2018	Onpattro (Patisiran) [36]	Alnylam	RNA	double-stranded siRNA against transthyretin mRNA	Hereditary Transthyretin-related Amyloidosis	*In-vivo*	FDA, EMA, UK, Japan, Canada, Switzerland, Brazil, Taiwan, Israel, Turkey	
2019	Collategene (Beperminogene perplasmid) [87]	AnGes	Plasmid	Human hepatocyte growth factor (*HGF*)	Critical Limb Ischemia	*In-vivo*	Japan	First Gene therapy product in Japan
2019	Zolgensma (Onasemnogene Abeparvovec-xioi) [88]	Novartis	AAV9	*SMN1*	Pediatric Spinal Muscular Atrophy	*In-vivo*	FDA, EMA, UK, Japan, Australia, Canada, Brazil, Israel, Taiwan, South Korea	Most expensive drug worldwide
2019	Zynteglo (Betibeglogene autotemcel) [89]	Bluebird Bio	lentivirus	βA-T87Q-globin (modified *β-globin* gene)	Adult transfusion-dependent ß-thalassemia	*Ex-vivo* (CD34 + cell)	EMA, UK	Later withdrawn from the market in 2022

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Approved gene therapy products

2020	Tecartus (brexucabtagene autoleucel/ KTE-X19) [92]	Kite Pharma (Gilead)	Retrovirus	*CD19* CAR	Relapsed/refractory mantle cell lymphoma	*Ex-vivo* (T cell)	FDA, EMA, UK	
2020	Libmeldy (Atidarsagene autotemcel) [93]	Orchard Therapeutics	Lentivirus	*ARSA* (arylsulfatase A) gene	Metachromatic Leukodystrophy	*Ex-vivo* (CD34 + cell)	EMA, UK	Autologous CD34 + cells encoding ARSA gene
2020	Comirnaty (Tozinameran) [94]	BioNTech	mRNA	lipid nanoparticle-formulated, nucleoside-modified mRNA encoding the SARS-CoV-2 spike (S) protein	COVID-19 vaccination	*In-vivo*	UK, Bahrain, Israel, Canada, FDA, Rwanda, Serbia, United Arab Emirates, Macao, Mexico, Kuwait, Singapore, Saudi Arabia, Chile, Switzerland, EMA, Colombia, Philippines, Australia, Hong Kong, Peru, South Korea, New Zealand, Japan, Brazil, Sri Lanka, Vietnam, South Africa, Thailand, Oman, Egypt, Malaysia	Pfizer-BioNTech COVID-19 mRNA Vaccine
2020	Spikevax (Moderna COVID-19 vaccine/ mRNA-1273, elasomeran) [95]	Moderna Therapeutics	mRNA	mRNA for pre-fusion stabilized Spike glycoprotein of SARS-CoV-2 virus	COVID-19 vaccination	*In-vivo*	FDA, Canada, Israel, EMA, Switzerland, Singapore, Qatar, Vietnam, UK, Philippines,	Moderna COVID- 19 vaccine

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Approved gene therapy products

2020	Givlaari (givosiran) [96]	Alnylam	RNA	siRNA aginst aminolevulinate synthase 1 (ALAS1) mRNA	Porphyria	*In-vivo*	FDA, EMA, UK, Canada, Switzerland, Brazil, Israel, Japan	
2020	Oxlumo (lumasiran) [97]	Alnylam	RNA	siRNA against hydroxyacid oxidase 1 (HAO1)	Primary hyperoxaluria type 1	*In-vivo*	EMA, UK, FDA, Brazil	
2020	Viltepso (viltolarsen) [98]	NS Pharma	DNA	Anti-sense oligonucleotide against exon 53 of dystrophin pre-mRNA	Duchenne Muscular Dystrophy	*In-vivo*	FDA, Japan	First DNA-based approved gene therapy product
2020	Leqvio (inclisiran/ ALN-PCSsc, ALN-60212) [99]	Alnylam	RNA	Anti-sense oligonucleotide (siRNA) against proprotein convertase subtilisin Kexin type 9 (PCSK9)	Primary hypercholesterolemia	*In-vivo*	EMA, UK, Australia, Canada, Israel, FDA	
2021	Breyanzi (lisocabtagene maraleucel) [100]	Celgene (Bristol Myers Squibb)	Retrovirus	CD19 CAR	Relapsed or refractory diffuse large B cell lymphoma; follicular lymphoma	*Ex-vivo* (T cell)	FDA, Japan	
2021	Abecma (Idecabtagene vicleuel) [101]	bluebird bio	Lentivirus	BCMA CAR	Multiple myeloma	*Ex-vivo* (T cell)	FDA, Canada, EMA, UK, Japan	
2021	ARI-0001 [102]	Hospital Clinic	Lentivirus	CD19 CAR	Adult relapsed/ refractory acute lymphoblastic leukemia	*Ex-vivo* (T cell)	Spain	
2021	Delytact (teserpaturev) (G47Δ) [103]	Daiichi Sankyo	HSV-1	Triple-mutated, replication-conditional oncolytic virus	Malignant Glioma	*In-vivo*	Japan	The first oncolytic virus for brain cancer
2021	Carteyva (Relma-cel/ relmacabtagene autoleucel) [104]	JW Therapeutics	Lentivirus	CD19 CAR	Relapsed or refractory diffuse large B cell lymphoma	*Ex-vivo* (T cell)	SFDA	
2021	Amondys 45 (casimersen/ SRP-4045) [105]	Sarepta Therapeutics	RNA	Antisense oligonucleotide against exon 45 of dystrophin gene	Duchenne Muscular Dystrophy	*In-vivo*	FDA	
2021	Skysona (elivaldogene autotemcel/ Lenti-D) [106]	bluebird bio	Lentivirus	*ABCD1* gene	Juvenile Cerebral Adrenoleukodystrophy	*Ex-vivo* (CD34 + cell)	EMA	Later withdrawn in 2022
2022	Carvykti (ciltacabtagene autoleucel) [107]	Legend Biotech	lentivirus	BCMA CAR	Relapsed or refractory multiple myeloma	*Ex-vivo* (T cell)	FDA	

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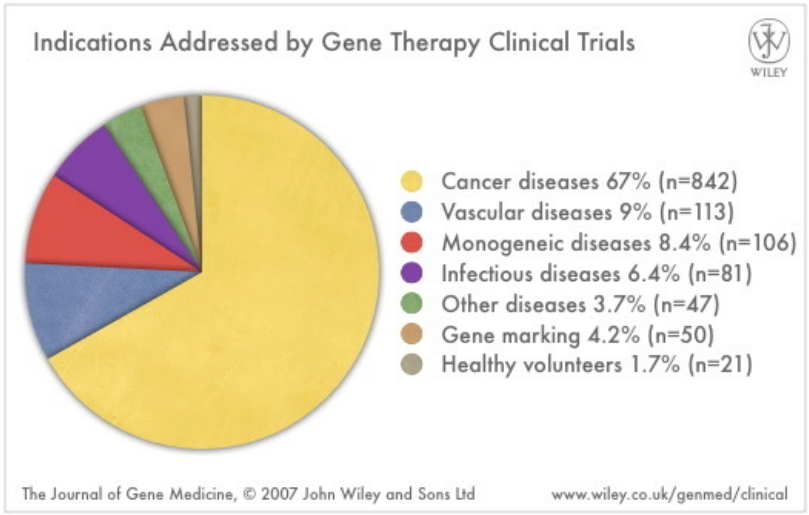
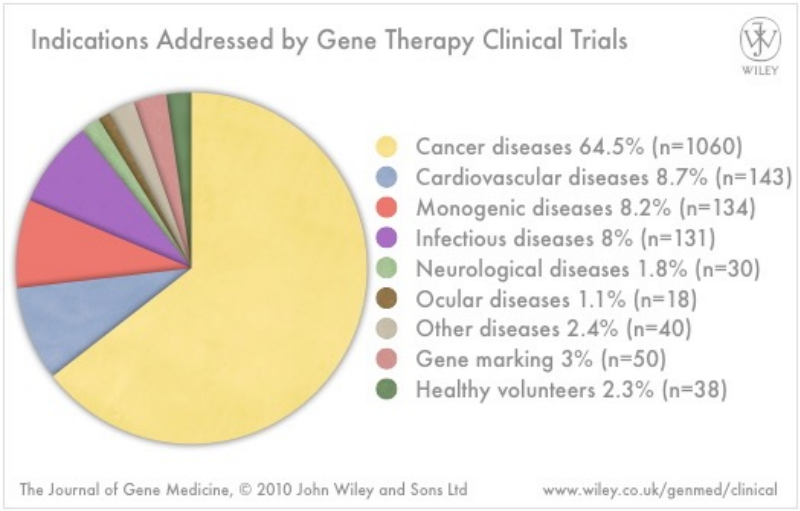
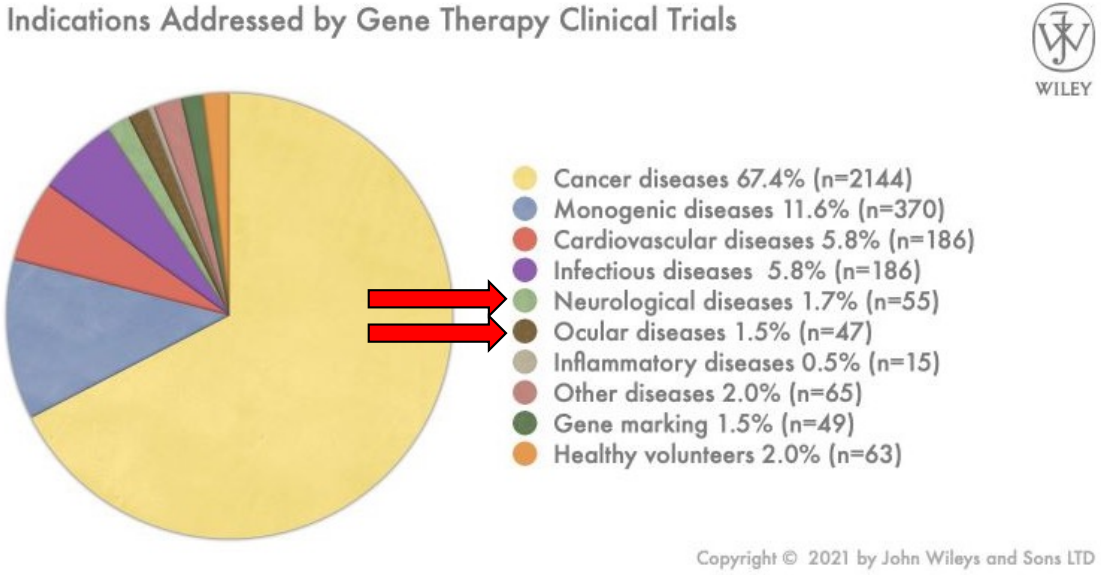
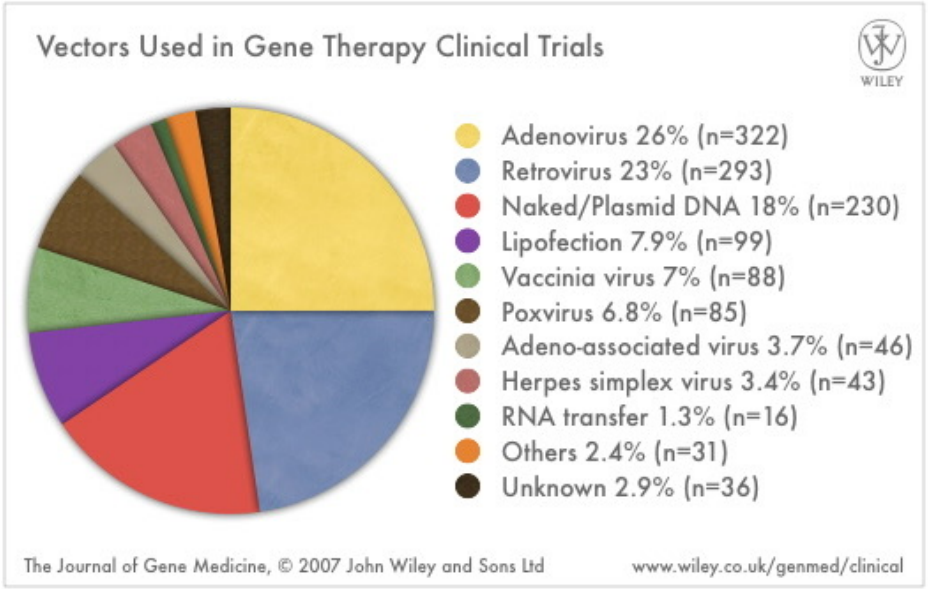
Which diseases with gene therapy

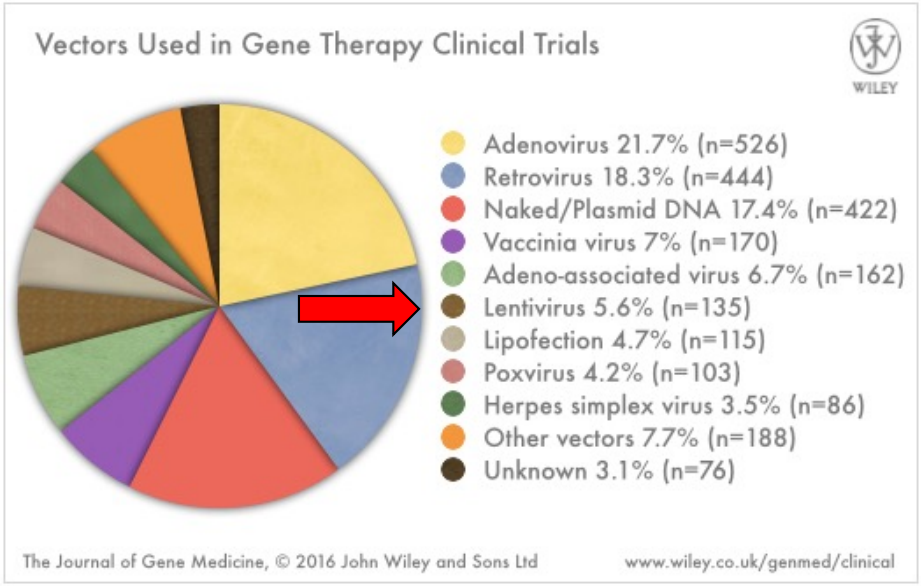


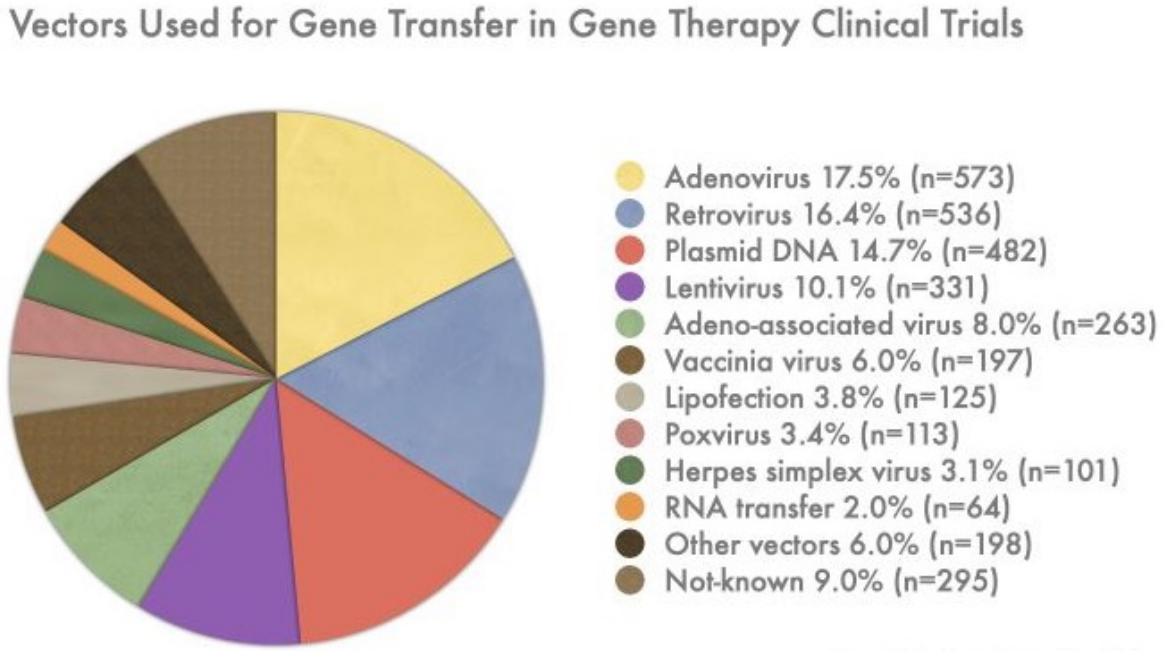




Which vectors for the genes







Trials in Italy

Trial ID	Title	disease/transgene	phase	virus/host cell	lab	closed
IT-0001	Treatment of Patients with Severe Combined Immunodeficiency Due to Adenosine Deaminase (ADA) Deficiency by Autologous Transplantation of Genetically Modified T Cells	ADA/ADA	I/II	retro PBL	bordignon milan	1995
IT-0002	Gene Transfer into Peripheral Blood Lymphocytes for In Vivo Immunomodulation of Donor Anti-Tumor Immunity in Patients Affected by Recurrent Disease After Allogeneic BMT	TK/graft versus host disease	I/II	retro PBL	bordignon milan	1995
IT-0003	Gene Transfer into Peripheral Blood Lymphocytes for In Vitro Immunosection and In Vivo Immunomodulation of Donor Anti-Tumor Immunity in Patients Affected by EBV-induced LPD Following Allogeneic BMT	TK/graft versus host disease	I/II	retro PBL	bordignon milan	1995
IT-0004	Active Immunization of Metastatic Melanoma Patients with Interleukin-4 Transfected, Allogeneic Melanoma Cells. A Phase I?II Study	IL4/melanoma	I/II	retro	cascinelli milan	1995
IT-0005	Gene Therapy for metastatic melanoma	IL2/melanoma	I/II	retro/tumor cell	cascinelli milan	open
IT-0006	Gene Therapy in Patients with Lymphoma and Leukemia	?/leukemia, limphoma	I	naked DNA/muscle cell	fazio rome	open
IT-0007	Active Immunization of Metastatic Melanoma Patients with Interleukin- 4 Transduced, Allogeneic Melanoma Cells. A Phase I? II Study	IL4/melanoma	I/II	retro/tumor cell	parminani milan	1997
IT-0008	Correction of ADA-SCID by stem cell gene therapy combined with nonmyeloblative conditionining	ADA/ADA	I		aiuti milan	open
IT-0009	Gene therapy in patients with melanoma	IL4/melanoma	I		maio aviano	open
IT-0010	Active immunization of metastatic melanoma patients with IL-2 or IL-4 gene transfected, allogeneic melanoma cells	IL2/melanoma	I		belli milan	1997
IT-0011	A phase I-II study of active vaccination with autologous T-lymphocytes transduced with HSV-TK and MAGE-A3 in patients with metastatic melanoma and expression of MAGE-A3	TK/melanoma	I/II	retro/autologous	parmiani milan	open
IT-0012	A Phase I Study to Evaluate the Safety/Tolerability and Immunogenicity of V-930 in Patients with Cancers Expressing HER-2 and/or CEA	HER CEA/Colrectal cancer, lung cancer	I/II	naked DNA/tumor cell	parmiani milan	closed
IT-0013	Pilot study of transfer of the FHIT gene into bronchial non-small cell lung cancers	Non-small cell lung cancer	I	Ad/ FHIT	parmiani milan	2002
IT-0014	A phase I/II study of active vaccination with autologous T-lymphocytes transduced with HSV-TK and MAGE-A3 in patients with metastatic melanoma and expression of MAGE-A3	TK/melanoma	I/II	retro/autologous	russo milan	open
IT-0015	Study of the safety and efficacy of hematopoietic stem cells transduced with RevM10polAS (RevM10polAS HSCIP) as therapy for HIV-1 infected persons	HIV-1 RevM10 HIV-1 polAS/HIV	I/II	retro/autologous	lazzarin milan	2003

http://www.abedia.com/wiley/index.html

Trials in Italy (registered 2013)

Trial ID	Title	disease/transgene	phase	virus/host cell	lab	closed
IT-0016	ADA Gene Transfer Into Hematopoietic Stem/Progenitor Cells for the Treatment of ADA-SCID	ADA/ADA	I/II	retro/CD34	roncarolo milan	open
IT-0017	phase III study: infusion of donor lymphocytes transduced with the suicide gene gene HSV-TK after transplantation of allogenic T-depleted stem cells from a haploidentical donor in patients with haematological malignancies	TK/Leukemia	III	HSV		open
IT-0018	Phase I/II study of hematopoietic stem cell gene therapy with Lentiviral Vectors for the treatment of Metachromatic Leukodystrophy	Arysulfate A/Metachromatic Leukodystrophy	I/II	lenti/-	biffi milan	open
IT-0019	Phase I/II study of hematopoietic stem cell gene therapy with Lentiviral Vectors for the treatment of Wiskott Aldrich Syndrome	/WAS gene	I/II		aiuti milan	open
IT-0020	TK008 Randomized Phase III Trial of Haploidentical HCT With or Without an Add Back Strategy of HSV-Tk Donor Lymphocytes in Patients With High Risk Acute Leukemia	leukemia/tyrosinase	III	HSV	ciceri milan	open
IT-0021	Phase Ib Study to Assess the Safety and Immunogenicity of a Novel HCV Vaccine, Based on the Sequential Injection of Ad6NSmut and MVA-NSmut, Given in Combination With PEG-Interferon Alfa Plus Ribavirin for Re-treatment of Chronic Hepatitis C	HCV/Nsmut	I	Ad-ankara vaccine	brunetto pisa	open
IT-0022	Phase I Study of CaspaCIDe T Cells From an HLA-partially Matched Family Donor After Negative Selection of TCR Alpha Beta T Cells in Pediatric Patients Affected by Hematological Disorders	Inducible Caspase 9 Suicide Gene/AP1903	I/II	Retro/T cells	Locatelli Rome	open
IT-0023-IT0024	Targeted Genome Editing in Human Repopulating Haematopoietic Stem Cells	IL-2RG	I	-/CD34+	Genovese Milan	2014
IT-0025	A Phase I/II Study Evaluating Safety and Efficacy of Autologous Hematopoietic Stem Cells Genetically Modified With GLOBE Lentiviral Vector Encoding for the Human Beta-globin Gene for the Treatment of Patients Affected by Transfusion Dependent Beta-thalassemia	Human β-Globin	I/II	Lentivectors	aiuti milan	open
IT-0026	A Multicentric, Exploratory, Non-randomised, Non-controlled, Prospective, Open-label Phase II Study Evaluating Safety and Efficacy of IBU, G-CSF and Plerixafor as Stem Cell Mobilization Regimen in Patients Affected by X-CGD	gp91phox	II	Lentivectors	Ciceri milan	open
IT-0016	ADA Gene Transfer Into Hematopoietic Stem/Progenitor Cells for the Treatment of ADA-SCID	ADA/ADA	I/II	retro/CD34	roncarolo milan	open
IT-0017	phase III study: infusion of donor lymphocytes transduced with the suicide gene gene HSV-TK after transplantation of allogenic T-depleted stem cells from a haploidentical donor in patients with haematological malignancies	TK/Leukemia	III	HSV		open
IT-0018	Phase I/II study of hematopoietic stem cell gene therapy with Lentiviral Vectors for the treatment of Metachromatic Leukodystrophy	Arysulfate A/Metachromatic Leukodystrophy	I/II	lenti/-	biffi milan	open
IT-0019	Phase I/II study of hematopoietic stem cell gene therapy with Lentiviral Vectors for the treatment of Wiskott Aldrich Syndrome	/WAS gene	I/II		aiuti milan	open
IT-0020	TK008 Randomized Phase III Trial of Haploidentical HCT With or Without an Add Back Strategy of HSV-Tk Donor Lymphocytes in Patients With High Risk Acute Leukemia	leukemia/tyrosinase	III	HSV	ciceri milan	open
IT-0021	Phase Ib Study to Assess the Safety and Immunogenicity of a Novel HCV Vaccine, Based on the Sequential Injection of Ad6NSmut and MVA-NSmut, Given in Combination With PEG-Interferon Alfa Plus Ribavirin for Re-treatment of Chronic Hepatitis C	HCV/Nsmut	I	Ad-ankara vaccine	brunetto pisa	open

Trials in Italy

Trial ID	Title	disease/transgene	phase	virus/host cell	lab	closed
IT-0027	A Phase I/II Open Label, Dose Escalation, Safety Study in Subjects With Mucopolysaccharidosis Type VI (MPS VI) Using Adeno-Associated Viral Vector 8 to Deliver the Human ARSB Gene to Liver	ARSB	I/II	AAV/Hepatocytes	Brunetti-Pierri Naples	open
IT-0028	A Long-term Safety and Efficacy follow-on Study in Participants With Transfusion Dependent Beta-thalassemia Who Have Previously Received GSK2696277 (Autologous Hematopoietic Stem Cells Genetically Modified With GLOBE Lentiviral Vector Encoding for the Human Beta-globin Gene) and Completed the TIGET-BTHAL Study	Beta globin	I/II	Lentivectors	unknown	open
IT-0029	A Single Arm, Open Label, Clinical Study of Cryopreserved Autologous CD34+ Cells Transduced With Lentiviral Vector Containing Human ARSA cDNA (GSK2696274), for the Treatment of Early Onset Metachromatic Leukodystrophy (MLD)	ARSA	III	Lenti/CD34+	San Raffaelel-TIGET Milan	open
IT-0030	Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID) Registry for Patients Treated With Strimvelis (or GSK2696273) Gene Therapy: Long-Term Prospective, Non-Interventional Follow-up of Safety and Effectiveness	Adenosine deaminase (ADA)	IV	Retro/CD34+	Milan	open
IT-0031	Phase I/II Study of Anti-GD2 Chimeric Antigen Receptor-Expressing T Cells in Pediatric Patients Affected by High Risk and/or Relapsed/Refractory Neuroblastoma	GD2 Chimeric Antigen Receptor	I/II	unknown	Locatelli Rome	open
IT-0032-IT0034	Phase I/II Study of Anti-CD19 Chimeric Antigen Receptor-Expressing T Cells in Pediatric Patients Affected by Relapsed/Refractory CD19+ Acute Lymphoblastic Leukemia and Non Hodgkin Lymphoma	CD19 Chimeric Antigen Receptor	I/II	unknown	Locatelli Rome	open
IT-0035	A Single Arm, Open-label Clinical Trial of Hematopoietic Stem Cell Gene Therapy With Cryopreserved Autologous CD34+ Cells Transduced With Lentiviral Vector Encoding WAS cDNA in Subjects With Wiskott-Aldrich Syndrome (WAS)	WAS cDNA	II	Lenti/CD34+	San Raffaelel-TIGET Milan	open
IT-0036	An Open Label, Non-randomized Trial to Evaluate the Safety and Efficacy of a Single Infusion of OTL-200 in Patients With Late Juvenile (LJ) Metachromatic Leukodystrophy (MLD).	ARSA	II	Lenti/CD34+	Fumagalli Milan	open
IT-0027	A Phase I/II Open Label, Dose Escalation, Safety Study in Subjects With Mucopolysaccharidosis Type VI (MPS VI) Using Adeno-Associated Viral Vector 8 to Deliver the Human ARSB Gene to Liver	ARSB	I/II	AAV/Hepatocytes	Brunetti-Pierri Naples	open
IT-0028	A Long-term Safety and Efficacy follow-on Study in Participants With Transfusion Dependent Beta-thalassemia Who Have Previously Received GSK2696277 (Autologous Hematopoietic Stem Cells Genetically Modified With GLOBE Lentiviral Vector Encoding for the Human Beta-globin Gene) and Completed the TIGET-BTHAL Study	Beta globin	I/II	Lentivectors	unknown	open
IT-0029	A Single Arm, Open Label, Clinical Study of Cryopreserved Autologous CD34+ Cells Transduced With Lentiviral Vector Containing Human ARSA cDNA (GSK2696274), for the Treatment of Early Onset Metachromatic Leukodystrophy (MLD)	ARSA	III	Lenti/CD34+	San Raffaele-TIGET Milan	open
IT-0030	Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID) Registry for Patients Treated With Strimvelis (or GSK2696273) Gene Therapy: Long-Term Prospective, Non-Interventional Follow-up of Safety and Effectiveness	Adenosine deaminase (ADA)	IV	Retro/CD34+	Milan	open
IT-0031	Phase I/II Study of Anti-GD2 Chimeric Antigen Receptor-Expressing T Cells in Pediatric Patients Affected by High Risk and/or Relapsed/Refractory Neuroblastoma	GD2 Chimeric Antigen Receptor	I/II	unknown	Locatelli Rome	open
IT-0032-IT0034	Phase I/II Study of Anti-CD19 Chimeric Antigen Receptor-Expressing T Cells in Pediatric Patients Affected by Relapsed/Refractory CD19+ Acute Lymphoblastic Leukemia and Non Hodgkin Lymphoma	CD19 Chimeric Antigen Receptor	I/II	unknown	Locatelli Rome	open
IT-0035	A Single Arm, Open-label Clinical Trial of Hematopoietic Stem Cell Gene Therapy With Cryopreserved Autologous CD34+ Cells Transduced With Lentiviral Vector Encoding WAS cDNA in Subjects With Wiskott-Aldrich Syndrome (WAS)	WAS cDNA	II	Lenti/CD34+	San Raffaelel-TIGET Milan	open
IT-0036	An Open Label, Non-randomized Trial to Evaluate the Safety and Efficacy of a Single Infusion of OTL-200 in Patients With Late Juvenile (LJ) Metachromatic Leukodystrophy (MLD).	ARSA	II	Lenti/CD34+	Fumagalli Milan	open

DNA as a drug, ideally...pros

- long term
- treatment of the cause
- specificity
- no side effects

Potential risks of gene therapy

- Insertional mutagenesis leading to cancer
- Recombination of disabled vector resulting in environmental pollution by infectious recombinant virus
- Toxic shock caused by viraemia
- Transfer of non-viral exogenous material
- Contamination with other deleterious viruses or organisms
- Physiological effects of over-expression
- Germ-line transduction?