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Supplemental information

25 years of maturation:

A systematic review of RNAi in the clinic

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Supplemental Materials

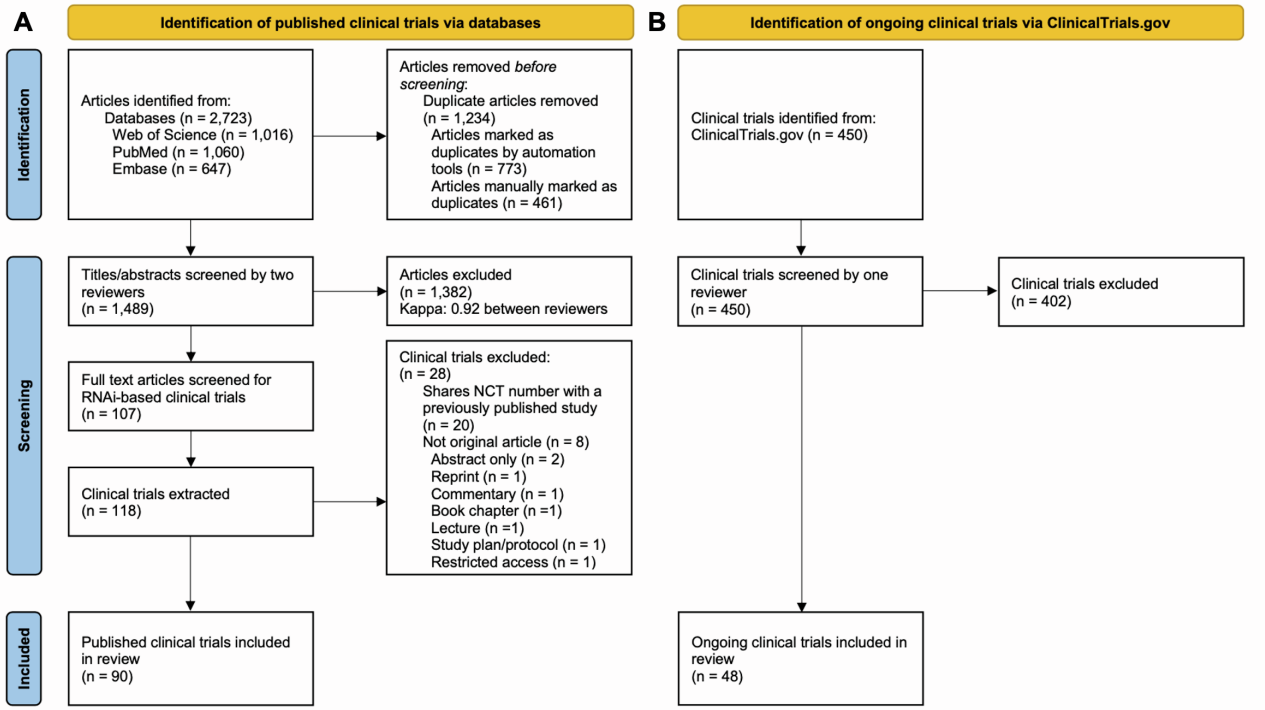

Figure S1: Flow diagram of the selection process. (A) Published clinical trials included in this review. **(B)** Ongoing clinical trials included in this review. *Adapted from:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews.[1]

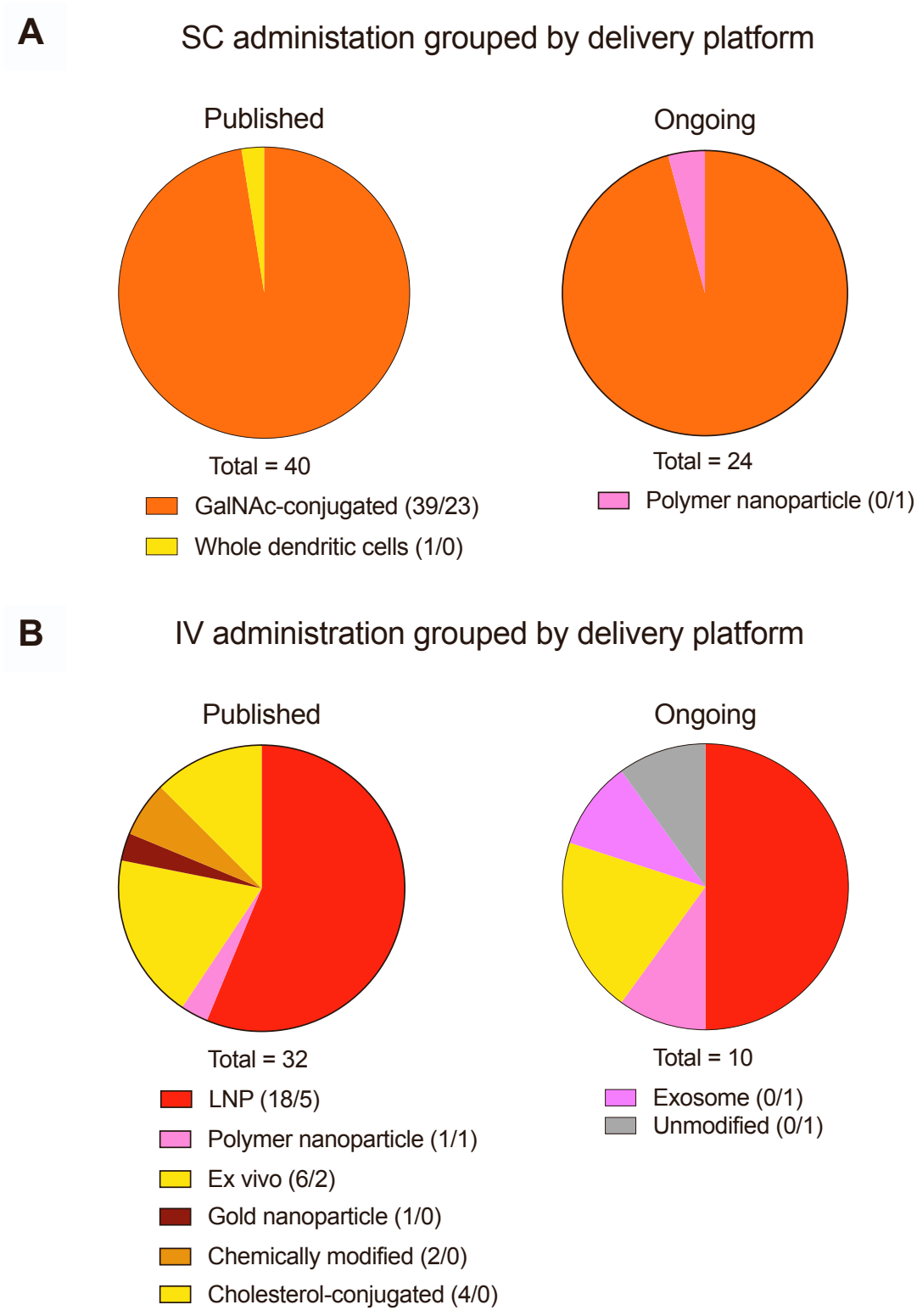

Figure S2: SC or IV administration grouped by delivery platform. (A-B) Overall distribution of the types of delivery platforms used in combination with SC or IV administration in the published/ongoing clinical trials. Color coded annotations are included for every distribution.

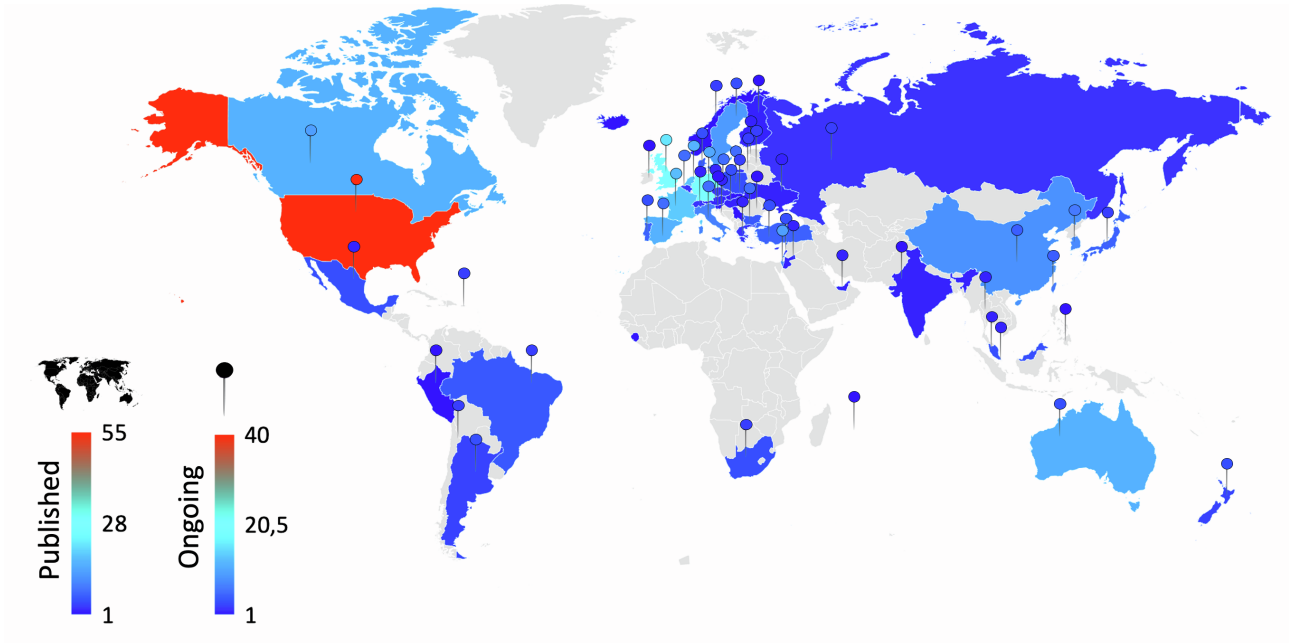

Figure S3: The world of clinical RNAi. Heat map showing the countries from where the patients of the published and ongoing RNAi-based clinical trials have been or are being recruited from. Color-coded annotations are included on the left side. “Red” correlates with the highest number of studies recruiting patients from the involved country, whereas “dark blue” correlates with the lowest number of studies. Grey color indicate that no patients were recruited from the involved country. The countries involved in the published clinical trials are represented by the color on the map, whereas the countries involved in the ongoing clinical trials are represented by the colors on the pins on the map.

Table S1: Overview of the included published cinical trials. Characteristics of the 90 published clinical trials included in this review. The * indicates that the NCT number was not found in the article, but was found manually by the reviewers, who screened the clinical trials. The - indicates that no NCT was found in the article nor manually.

Nr.	Name of first author	Title	Year of publication	NCT
1	DeVincenzo, John	Evaluation of the safety, tolerability and pharmacokinetics of ALN-RSV01, a novel RNAi antiviral therapeutic directed against respiratory syncytial virus (RSV)	2008	-
2	Wyszko, Eliza	A multivariate analysis of patients with brain tumors treated with ATN-RNA	2008	-
3	DeVincenzo, John	A randomized, double-blind, placebo-controlled study of an RNAi-based therapy directed against respiratory syncytial virus	2010	NCT00496821
4	DiGiusto, David L.	RNA-Based Gene Therapy for HIV With Lentiviral Vector-Modified CD34(+) Cells in Patients Undergoing Transplantation for AIDS-Related Lymphoma	2010	-
5	Leachman, Sancy A.	First-in-human Mutation-targeted siRNA Phase Ib Trial of an Inherited Skin Disorder	2010	NCT00716014
6	Kaiser, Peter K.	RNAi-Based Treatment for Neovascular Age-Related Macular Degeneration by Sirna-027	2010	NCT00363714
7	Gish, Robert G	RNA interference and its potential applications to chronic HBV treatment: results of a Phase I safety and tolerability study	2011	-
8	Zamora, Martin R.	RNA Interference Therapy in Lung Transplant Patients Infected with Respiratory Syncytial Virus	2011	NCT00658086
9	Nguyen, Quan Dong	Dose-Ranging Evaluation of Intravitreal siRNA PF-04523655 for Diabetic Macular Edema (the DEGAS Study)	2012	NCT00701181
10	Nguyen, Quan Dong	Evaluation of the siRNA PF-04523655 versus Ranibizumab for the Treatment of Neovascular Age-related Macular Degeneration (MONET Study)	2012	NCT00713518
11	Nguyen, Quan Dong	Phase 1 dose-escalation study of a siRNA targeting the RTP801 gene in age-related macular degeneration patients	2012	NCT00725686
12	Senzer, Neil	Phase I Trial of "bi-shRNAi(furin)/GMCSF DNA/Autologous Tumor Cell" Vaccine (FANG) in Advanced Cancer	2012	-

13	Coelho, Teresa	Safety and Efficacy of RNAi Therapy for Transthyretin Amyloidosis	2013	NCT01148953
14	Coelho, Teresa	Safety and Efficacy of RNAi Therapy for Transthyretin Amyloidosis	2013	NCT01559077
15	Tabernero, Josep	First-in-Humans Trial of an RNA Interference Therapeutic Targeting VEGF and KSP in Cancer Patients with Liver Involvement	2013	NCT00882180
16	Tabernero, Josep	First-in-Humans Trial of an RNA Interference Therapeutic Targeting VEGF and KSP in Cancer Patients with Liver Involvement	2013	NCT01158079
17	Fitzgerald, Kevin	Effect of an RNA interference drug on the synthesis of proprotein convertase subtilisin/kexin type 9 (PCSK9) and the concentration of serum LDL cholesterol in healthy volunteers: a randomised, single-blind, placebo-controlled, phase 1 trial	2014	NCT01437059
18	Moreno-Montanes, Javier	Phase I Clinical Trial of SYL040012, a Small Interfering RNA Targeting beta-Adrenergic Receptor 2, for Lowering Intraocular Pressure	2014	NCT00990743
19	Nemunaitis, John	Summary of bi-shRNA(furin)/GM-CSF Augmented Autologous Tumor Cell Immunotherapy (FANG (TM)) in Advanced Cancer of the Liver	2014	-
20	Schultheis, Beate	First-in-Human Phase I Study of the Liposomal RNA Interference Therapeutic Atu027 in Patients With Advanced Solid Tumors	2014	NCT00938574
21	Zuckerman, Jonathan E.	Correlating animal and human phase Ia/Ib clinical data with CALAA-01, a targeted, polymer-based nanoparticle containing siRNA	2014	NCT00689065*
22	Barve, Minal	Phase 1 Trial of Bi-shRNA STMN1 BIV in Refractory Cancer	2015	NCT01505153*
23	Golan, Talia	RNAi therapy targeting KRAS in combination with chemotherapy for locally advanced pancreatic cancer patients	2015	NCT01188785
24	Suhr, Ole B.	Efficacy and safety of patisiran for familial amyloidotic polyneuropathy: a phase II multi-dose study	2015	NCT01617967
25	Gottlieb, Jens	ALN-RSV01 for prevention of bronchiolitis obliterans syndrome after respiratory syncytial virus. infection in lung transplant recipients	2016	NCT01065935

26	Oh, Jonathan	Phase II study of Vigil DNA engineered immunotherapy as maintenance in advanced stage ovarian cancer	2016	-
27	Dunning, Jake	Experimental Treatment of Ebola Virus Disease with TKM-130803: A Single-Arm Phase 2 Clinical Trial	2016	-
28	Adams, David	Trial design and rationale for APOLLO, a Phase 3, placebo-controlled study of patisiran in patients with hereditary ATTR amyloidosis with polyneuropathy	2017	NCT01960348
29	Beg, Muhammad S.	Phase I study of MRX34, a liposomal miR-34a mimic, administered twice weekly in patients with advanced solid tumors	2017	NCT01829971
30	Fitzgerald, Kevin	A Highly Durable RNAi Therapeutic Inhibitor of PCSK9	2017	NCT02314442
31	Pasi, K. John	Targeting of Antithrombin in Hemophilia A or B with RNAi Therapy	2017	NCT02035605
32	Ray, Kausik K.	Inclisiran in Patients at High Cardiovascular Risk with Elevated LDL Cholesterol	2017	NCT02597127
33	Schluep, Thomas	Safety, Tolerability, and Pharmacokinetics of ARC-520 Injection, an RNA Interference-Based Therapeutic for the Treatment of Chronic Hepatitis B Virus Infection, in Healthy Volunteers	2017	NCT01872065
34	Suzuki, Kenji	Phase 1 Clinical Study of siRNA Targeting Carbohydrate Sulphotransferase 15 in Crohn's Disease Patients with Active Mucosal Lesions	2017	-
35	van Zandwijk, Nico	Safety and activity of microRNA-loaded minicells in patients with recurrent malignant pleural mesothelioma: a first-in-man, phase 1, open-label, dose-escalation study	2017	NCT02369198
36	Wooddell, Christine	RNAi-based treatment of chronically infected patients and chimpanzees reveals that integrated hepatitis B virus DNA is a source of HBsAg	2017	NCT02065336*
37	Zimmermann, Tracy S.	Clinical Proof of Concept for a Novel Hepatocyte-Targeting GalNAc-siRNA Conjugate	2017	NCT01814839
38	Turner, Alice M.	Hepatic-targeted RNA interference provides robust and persistent knockdown of alpha-1 antitrypsin levels in ZZ patients	2018	NCT02363946
39	Wang, Danhong	Efficacy of intracellular immune checkpoint-silenced DC vaccine	2018	NCT01956630

40	El Dika, Imane	An Open-Label, Multicenter, Phase I, Dose Escalation Study with Phase II Expansion Cohort to Determine the Safety, Pharmacokinetics, and Preliminary Antitumor Activity of Intravenous TKM-080301 in Subjects with Advanced Hepatocellular Carcinoma	2019	NCT02191878
41	Kavita, Uma	A Fit-for-Purpose Method for the Detection of Human Antibodies to Surface-Exposed Components of BMS-986263, a Lipid Nanoparticle-Based Drug Product Containing a siRNA Drug Substance	2019	-
42	Sardh, Eliane	Phase 1 Trial of an RNA Interference Therapy for Acute Intermittent Porphyria	2019	NCT02452372
43	Delville, Marianne	Safety of CD34+ Hematopoietic Stem Cells and CD4+ T Lymphocytes Transduced with LVsh5/C46 in HIV-1 Infected Patients with High-Risk Lymphoma	2019	NCT03593187*
44	Brandts, Julia	Clinical implications and outcomes of the ORION Phase III trials	2020	NCT02963311
45	Brandts, Julia	Clinical implications and outcomes of the ORION Phase III trials	2020	NCT03060577
46	Brandts, Julia	Clinical implications and outcomes of the ORION Phase III trials	2020	NCT03851705
47	Brandts, Julia	Clinical implications and outcomes of the ORION Phase III trials	2020	NCT03060577
48	Coelho, Teresa	A phase II, open-label, extension study of long-term patisiran treatment in patients with hereditary transthyretin-mediated (hATTR) amyloidosis	2020	NCT01961921
49	Ray, Kausik K.	Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol	2020	NCT03399370
50	Ray, Kausik K.	Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol	2020	NCT03400800
51	Balwani, Manisha	Phase 3 Trial of RNAi Therapeutic Givosiran for Acute Intermittent Porphyria	2020	NCT03338816
52	Raal, Frederick J.	Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia	2020	NCT03397121
53	Judge, Daniel P.	Phase 3 Multicenter Study of Revusiran in Patients with Hereditary Transthyretin-Mediated (hATTR) Amyloidosis with Cardiomyopathy (ENDEAVOUR)	2020	NCT02319005

54	Wright, R. Scott	Effects of Renal Impairment on the Pharmacokinetics, Efficacy, and Safety of Inclisiran: An Analysis of the ORION-7 and ORION-1 Studies	2020	NCT03159416
55	Yuen, Man-Fung	RNA Interference Therapy With ARC-520 Results in Prolonged Hepatitis B Surface Antigen Response in Patients With Chronic Hepatitis B Infection	2020	NCT02604199
56	Yuen, Man-Fung	RNA Interference Therapy With ARC-520 Results in Prolonged Hepatitis B Surface Antigen Response in Patients With Chronic Hepatitis B Infection	2020	NCT02604212
57	Chen, Li-Yun	Successful application of anti-CD19 CAR-T therapy with IL-6 knocking down to patients with central nervous system B-cell acute lymphocytic leukemia	2020	NCT03064269
58	Schultheis, Beate	Safety, efficacy and pharcacokinetics of targeted therapy with the liposomal RNA interference therapeutic atu027 combined with gemcitabine in patients with pancreatic adenocarcinoma. A randomized phase Ib/IIa study	2020	NCT01808638
59	Garrelfs, Sander F.	Lumasiran, an RNAi Therapeutic for Primary Hyperoxaluria Type 1	2021	NCT03681184
60	Esrick, Erica B.	Post-Transcriptional Genetic Silencing of BCL11A to Treat Sickle Cell Disease	2021	NCT03282656
61	Badri, Prajakta	Pharmacokinetic and Pharmacodynamic Properties of Cemdisiran, an RNAi Therapeutic Targeting Complement Component 5, in Healthy Subjects and Patients with Paroxysmal Nocturnal Hemoglobinuria	2021	NCT02352493
62	Gupta, Sheha V. Gupta	Clinical and Preclinical Single-Dose Pharmacokinetics of VIR-2218, an RNAi Therapeutic Targeting HBV Infection	2021	NCT03672188
63	Kumthekar, Priya	A first-in-human phase 0 clinical study of RNA interference-based spherical nucleic acids in patients with recurrent glioblastoma	2021	NCT03020017
64	Adams, David	Long-term safety and efficacy of patisiran for hereditary transthyretin-mediated amyloidosis with polyneuropathy: 12-month results of an open-label extension study	2021	NCT02510261

65	Frishberg, Yaacov	Phase 1/2 Study of Lumasiran for Treatment of Primary Hyperoxaluria Type 1 A Placebo-Controlled Randomized Clinical Trial	2021	NCT02706886
66	Thielmann, Matthias	Teprasiran, a Small Interfering RNA, for the Prevention of Acute Kidney Injury in High-Risk Patients Undergoing Cardiac Surgery A Randomized Clinical Study	2021	NCT02610283
67	Vassiliou, Daphne	A Drug-Drug Interaction Study Evaluating the Effect of Givosiran, a Small Interfering Ribonucleic Acid, on Cytochrome P450 Activity in the Liver	2021	NCT03505853
68	To-Figueras, Jordi	Dysregulation of homocysteine homeostasis in acute intermittent porphyria patients receiving heme arginate or givosiran	2021	-
69	Gane, Ed	JNJ-73763989 pharmacokinetics and safety: Liver-targeted siRNAs against hepatitis B virus, in Japanese and non-Japanese healthy adults, and combined with JNJ-56136379 and a nucleos(t)ide analogue in patients with chronic hepatitis B	2022	NCT03365947
70	Gane, Ed	JNJ-73763989 pharmacokinetics and safety: Liver-targeted siRNAs against hepatitis B virus, in Japanese and non-Japanese healthy adults, and combined with JNJ-56136379 and a nucleos(t)ide analogue in patients with chronic hepatitis B	2022	NCT04002752
71	Gong, Wen-Jie	Investigation of the risk factors to predict cytokine release syndrome in relapsed or refractory B-cell acute lymphoblastic leukemia patients receiving IL-6 knocking down anti-CD19 chimeric antigen receptor T-cell therapy	2022	NCT03275493
72	Hoppe, Bernd	Safety, pharmacodynamics, and exposure-response modeling results from a first-in-human phase 1 study of nedosiran (PHYOX1) in primary hyperoxaluria	2022	NCT03392896
73	Kallend, David	An evaluation of a supratherapeutic dose of inclisiran on cardiac repolarization in healthy volunteers: A phase I, randomized study	2022	-
74	Koren, Michael J.	Preclinical development and phase 1 trial of a novel siRNA targeting lipoprotein(a)	2022	NCT03626662
75	Lawitz, Eric J.	BMS-986263 in patients with advanced hepatic fibrosis: 36-week results from a randomized, placebo-controlled phase 2 trial	2022	NCT03420768

76	Nissen, Steven E.	Single Ascending Dose Study of a Short Interfering RNA Targeting Lipoprotein(a) Production in Individuals With Elevated Plasma Lipoprotein(a) Levels	2022	NCT04606602
77	Rejman, M. Doortje	Rationale and design of two trials assessing the efficacy, safety, and tolerability of inclisiran in adolescents with homozygous and heterozygous familial hypercholesterolaemia	2022	NCT04659863
78	Rejman, M. Doortje	Rationale and design of two trials assessing the efficacy, safety, and tolerability of inclisiran in adolescents with homozygous and heterozygous familial hypercholesterolaemia	2022	NCT04652726
79	Rocconi, Rodney P.	Proof of principle study of sequential combination atezolizumab and Vigil in relapsed ovarian cancer	2022	NCT03073525
80	Sohn, Winnie	Pharmacokinetics, Pharmacodynamics, and Tolerability of Olpasiran in Healthy Japanese and Non-Japanese Participants: Results from a Phase I, Single-dose, Open-label Study	2022	-
81	Strnad, Pavel	Fazirsiran for Liver Disease Associated with Alpha(1)-Antitrypsin Deficiency	2022	NCT03946449
82	Sas, David J.	Phase 3 trial of lumasiran for primary hyperoxaluria type 1: A new RNAi therapeutic in infants and young children	2022	NCT03905694
83	Adams, David	Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial	2022	NCT03759379
84	Kallend, David	Pharmacokinetics and pharmacodynamics of inclisiran, a small interfering RNA therapy, in patients with hepatic impairment	2022	-
85	O'Donoghue, Michelle	Small Interfering RNA to Reduce Lipoprotein(a) in Cardiovascular Disease	2022	NCT04270760
86	Schmidt, Hartmu H.	Patisiran treatment in patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy after liver transplantation	2022	NCT03862807
87	Ventura, Paolo	Efficacy and safety of givosiran for acute hepatic porphyria: 24-month interim analysis of the randomized phase 3 ENVISION study	2022	NCT03338816
88	Li, Haiyan	Pharmacokinetics, Safety, and Tolerability of the siRNA JNJ-73763989 in Healthy Chinese Adult Participants	2023	NCT04586439

89	Mak, Lung-Yi	A phase I/II study of ARO-HSD, an RNA interference therapeutic, for the treatment of non-alcoholic steatohepatitis	2023	NCT04202354
90	Michael, Mini	Lumasiran for Advanced Primary Hyperoxaluria Type 1: Phase 3 ILLUMINATE-C Trial	2023	NCT04152200

Table S2: Overview of the included ongoing clinical trials. Characteristics of the 48 ongoing clinical trials included in this review.

Nr.	Sponsor	Title	Year of clinical start date	NCT
1	Genzyme, a Sanofi Company	An Open-label Extension Study of an Investigational Drug, Fitusiran, in Patients with Moderate or Severe Hemophilia A or B	2015	NCT02554773
2	M.D. Anderson Cancer Center	EphA2 siRNA in Treating Patients With Advanced or Recurrent Solid Tumors	2015	NCT01591356
3	AIDS Malignancy Consortium	Gene Therapy in Treating Patients With Human Immunodeficiency Virus-Related Lymphoma Receiving Stem Cell Transplant	2016	NCT02797470
4	Gradalis, Inc.	Pbi-shRNA™ EWS/FLI1 Type 1 LPX in Subjects With Advanced Ewing's Sarcoma	2016	NCT02736565
5	Gradalis, Inc.	Trial of Atezolizumab and Vigil for Advanced Gynecological Cancers (A Companion Study to CL-PTL-119)	2017	NCT03073525
6	University of Oxford	A Randomized Trial Assessing the Effects of Inclisiran on Clinical Outcomes Among People With Cardiovascular Disease (ORION-4)	2018	NCT03705234
7	Alnylam Pharmaceuticals	A Study to Evaluate Lumasiran in Children and Adults With Primary Hyperoxaluria Type 1 (ILLUMINATE-A)	2018	NCT03681184
8	Gradalis, Inc	Vigil + Irinotecan and Temozolomide in Ewing's Sarcoma (VITA)	2018	NCT03495921
9	Alnylam Pharmaceuticals	An Extension Study of an Investigational Drug, Lumasiran (ALN-GO1), in Patients With Primary Hyperoxaluria Type 1	2018	NCT03350451
10	Boston Children's University	Gene Transfer for Sickle Cell Disease	2018	NCT03282656
11	Silenseed Ltd	A Phase 2 Study of siG12D LODER in Combination With Chemotherapy in Patients With Locally Advanced Pancreatic Cancer (PROTACT)	2018	NCT01676259
12	Alnylam Pharmaceuticals	HELIOS-B: A Study to Evaluate Vutrisiran in Patients With Transthyretin Amyloidosis With Cardiomyopathy	2019	NCT04153149

13	Dicerna Pharmaceuticals, Inc.	Long Term Extension Study in Patients With Primary Hyperoxaluria (PHYOX3)	2019	NCT04042402
14	Hugel	The Hypertrophic Scar Prevention of BMT101	2019	NCT04012099
15	Alnylam Pharmaceuticals	APOLLO-B: A Study to Evaluate Patisiran in Participants With Transthyretin Amyloidosis With Cardiomyopathy (ATTR Amyloidosis With Cardiomyopathy	2019	NCT03997383
16	Alnylam Pharmaceuticals	A Study of Lumasiran in Infants and Young Children With Primary Hyperoxaluria Type 1 (ILLUMINATE-B)	2019	NCT03905694
17	Nitto BioPharma, Inc.	A Study of NBF-006 in Non-Small Cell Lung, Pancreatic, or Colorectal Cancer	2019	NCT03819387
18	Novartis Pharmaceuticals	Trial to Assess the Effect of Long-Term Dosing of Inclisiran in Subjects With High CV Risk and Elevated LDL-C (ORION-8)	2019	NCT03814187
19	Sirnaomics	A Study of STP707 Administered by IV in Healthy Subjects	2020	NCT05309915
20	InteRNA	First-in-Human Study of INT-1B3 in Patients With Advanced Solid Tumors	2020	NCT04675996
21	Alnylam Pharmaceuticals	A Study of ALN-HSD in Healthy Adult Subjects and Adult Patients With Nonalcoholic Steatohepatitis (NASH)	2020	NCT04565717
22	Hoffmann-La Roche	A Trial To Evaluate The Efficacy And Safety Of Multiple Combination Therapies In Participants With Chronic Hepatitis B (Piranga)	2020	NCT04225715
23	Alnylam Pharmaceuticals	A Study to Evaluate Lumasiran in Patients With Advanced Primary Hyperoxaluria Type 1 (ILLUMINATE-C)	2020	NCT04152200
24	4D Molecular Therapeutics	4D-150 in Patients With Neovascular (Wet) Age-Related Macular Degeneration	2021	NCT05197270
25	Alnylam Pharmaceuticals	Zilebesiran as Add-on Therapy in Patients With Hypertension Not Adequately Controlled by a Standard of Care Antihypertensive Medication (KARDIA-2) (KARDIA-2)	2021	NCT05103332
26	Novartis Pharmaceuticals	Study of Inclisiran to Prevent Cardiovascular (CV) Events in Participants With Established Cardiovascular Disease (VICTORION-2P)	2021	NCT05030428

27	Alnylam Pharmaceuticals	A Study to Evaluate Efficacy and Safety of ALN-AGT01 in Patients With Mild To-Moderate Hypertension (KARDIA-1) (KARDIA-1)	2021	NCT04936035
28	Olix Pharmaceuticals, Inc.	Study to Evaluate Efficacy of OLX10010 in Reducing Recurrence of Hypertrophic Scarring After Scar Revision Surgery	2021	NCT04877756
29	Sirnaomics	A Study to Evaluate Safety, Efficacy of Intralesional Injection of STP705 in Patients With isSCC	2021	NCT04844983
30	Sirnaomics	A Study for Safety and Efficacy Evaluation of Various Doses of STP705 in Reducing Keloid Recurrence	2021	NCT04844840
31	Assembly Biosciences	A Study Evaluating Treatment Regimens Containing Vebicorvir (ABI-H0731) in Participants With Chronic Hepatitis B Infection	2021	NCT04820686
32	Sylentis, S.A.	Tivanisiran for Dry Eye in Subjects With Sjögren's Syndrome	2021	NCT04819269
33	Novartis Pharmaceuticals	Study of Efficacy and Safety of Inclisiran in Asian Participants With Atherosclerotic Cardiovascular Disease (ASCVD) or ASCVD High Risk and Elevated Low Density Lipoprotein Cholesterol (LDL-C)	2021	NCT04765657
34	Novartis Pharmaceuticals	Study to Evaluate Efficacy and Safety of Inclisiran in Adolescents With Homozygous Familial Hypercholesterolemia (ORION-13)	2021	NCT04659863
35	Novartis Pharmaceuticals	Study to Evaluate Efficacy and Safety of Inclisiran in Adolescents With Heterozygous Familial Hypercholesterolemia (ORION-16)	2021	NCT04652726
36	M.D. Anderson Cancer Center	iExosomes in Treating Participants With Metastatic Pancreas Cancer With KrasG12D Mutation	2021	NCT03608631
37	Oneness Biotech Co., Ltd.	A Phase I Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Single and Multiple Ascending Doses of Inhaled MBS-COV (SNS812) in Healthy Participants	2022	NCT05677893
38	Sylentis, S.A.	A Randomized, Double Masked, Parallel Group, Dose-finding Study to Evaluate SYL1801 in Patients With Neovascular Age-related Macular Degeneration (AMD)	2022	NCT05637255
39	Vir Biotechnology, Inc.	Effect of Hepatic Impairment on the Pharmacokinetics and Safety of VIR-2218 and VIR-3434	2022	NCT05484206

40	Sirnaomics	A Study to Evaluate Safety, Tolerability of Subcutaneous Injection in Adult Subjects Undergoing Abdominoplasty	2022	NCT05422378
41	Boston Children's University	A Gene Transfer Study Inducing Fetal Hemoglobin in Sickle Cell Disease (GRASP, BMT CTN 2001) (GRASP)	2022	NCT05353647
42	Sylentis, S.A.	Safety Study of Tivanisiran to Treat Dry Eye (FYDES)	2022	NCT05310422
43	Alnylam Pharmaceuticals	A Study to Evaluate ALN-XDH in Healthy Subjects and Patients With Gout	2022	NCT05256810
44	City of Hope Medical Center	CpG-STAT3 siRNA CAS3/SS3 and Localized Radiation Therapy for the Treatment of Relapsed/Refractory B-Cell NHL	2022	NCT04995536
45	Lemonex Inc.	A Study of Single Ascending Dose of LEM-S401 in Healthy Participants	2022	NCT04707131
46	Olix Pharmaceuticals, Inc.	Evaluation of OLX10212 in Patients With Neovascular Age-related Macular Degeneration	2023	NCT05643118
47	Silence Therapeutics plc	Evaluate SLN360 in Participants With Elevated Lipoprotein(a) at High Risk of Atherosclerotic Cardiovascular Disease Events	2023	NCT05537571
48	Silence Therapeutics plc	Study to Assess SLN124 in Patients With Polycythemia Vera (SLN)	2023	NCT05499013

Table S3: Studies presenting with two or more clinical trials with individual NCT number. Overview of the included studies presenting with two or more individual NCT numbers.

Title	Name of first author	Year of publication	Number of different NCT number	The different NCT numbers
Safety and Efficacy of RNAi Therapy for Transthyretin Amyloidosis	Coelho, Teresa	2013	2	NCT01148953 NCT01559077
First-in-Humans Trial of an RNA Interference Therapeutic Targeting VEGF and KSP in Cancer Patients with Liver Involvement	Tabernero, Josep	2013	2	NCT00882180 NCT01158079
Clinical implications and outcomes of the ORION Phase III trials	Brandts, Julia	2020	4	NCT02963311 NCT03060577 NCT03851705 NCT03060577
Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol	Ray, Kausik K.	2020	2	NCT03399370 NCT03400800
RNA Interference Therapy With ARC-520 Results in Prolonged Hepatitis B Surface Antigen Response in Patients With Chronic Hepatitis B Infection	Yuen, Man-Fung	2020	2	NCT02604199 NCT02604212
JNJ-73763989 pharmacokinetics and safety: Liver-targeted siRNAs against hepatitis B virus, in Japanese and non-Japanese healthy adults, and combined with JNJ-56136379 and a nucleos(t)ide analogue in patients with chronic hepatitis B	Gane, Ed	2022	2	NCT03365947 NCT04002752
Rationale and design of two trials assessing the efficacy, safety, and tolerability of inclisiran in adolescents with homozygous and heterozygous familial hypercholesterolaemia	Reijman, M. Doortje	2022	2	NCT04659863 NCT04652726

Table S4: Types of *ex vivo* delivery. Table summarizing the different types of *ex vivo* administration in the published/ongoing trials, shown in Fig. 4A**.** "Number" indicates the total number of studies utilizing the type of *ex vivo* administration.

Published clinical trials		**Ongoing clinical trials**	
Type	**Number**	**Type**	**Number**
DNA transfection of tumor cells	4	CD34+ cells transduced with lentivirus	3
T lymphocytes or hematopoietic stem cells transduced with lentivirus	3	DNA transfection of tumor cells	2
CAR-T cells transduced with lentivirus	1	Adenovirus transduction	1
Adenovirus transduction	2		
Minicells	1		

Table S5: Disease etiology. Diseases treated with RNAi therapeutics grouped by disease etiology. Information regarding the name of the RNAi-based drug, the number of times the RNAi therapeutic has been used in published/ongoing clinical trials, and total number of diseases treated with the RNAi therapeutics in published/ongoing clinical trials. The color of the boarder of the organ-boxes correlates with the color-coded annotations in Fig. 6. ASCVD, Atherosclerotic cardiovascular disease; hATTR, Hereditary ATTR amyloidosis; RSV, Respiratory Syncytial Virus; HBV, hepatitis B virus; HIV-1, Human Immunodeficiency Virus-1; wAMD, wet Age-dependent Macular Degeneration; DME, Diabetic Macular Edema; IOP, Intraocular Pressure.

Organ	Disease	Name of RNAi-based drug and number included in published/ongoing clinical trials	Total number of diseases treated in published/ongoing clinical trials
Cardiovascular			19/9
	ASCVD	Inclisiran	15/6
	Elevated Apolipoprotein A (cardiovascular disease) and hypercholesterolemia	Olpasiran: 3/0	4/1
		SLN360: 1/1	
	Hypertension	ALALN-AGT01	0/2
Tumor			19/11
	Cancer with CNS involvement	ATN-RNA:1	2/0
		NU-0129: 1	
	Advanced cancer	FANG/VIGIL: 2/0	6/4
		Atu27:1/0	
		CALAA-01: 1/0	
		STMN1: 1/0	
		MRX34: 1/0	
		EphA2 siRNA: 0/1	
		NBF-006: 0/1	
		INT-1B3: 0/1	
		ALN-HSD: 0/1	
	Cancer with liver involvement	ALN-VSP: 2/0	3/0
		TKM-080301: 1/0	
	Recurrent Malignant Pleural Mesothelioma	TargomiR	1/0
	Central nervous system B-cell acute lymphocytic leukemia	ssCART-19s	1/0
	Cancer with pancreas involvement	siG12D-LODER: 1/2	2/2
		ATU027: 1	

	Relapsed or Refractory B-cell acute lymphoblastic leukemia	ssCAR-T19	1/0
	Acute leukemia	Ad-siSSF-DC	1/0
	Recurrent B-Cell Non-Hodgkin Lymphoma	CAS3/SS3	0/1
	Cancer with female reproductive organs involved	FANG/VIGIL: 2/1	2/1
	Squamous Cell Carcinoma	STP705	0/1
	Ewings Sarcoma	pbi-shRNA: 0/1	0/2
		Vigil: 0/1	
Liver			18/3
	hATTR	Patisiran: 6/1	10/2
		ALN-TTR01: 1/0	
		Revusiran: 2/0	
		Vutrisiran: 1/1	
	Acute hepatic porphyrias	Givosiran	5/0
	Advanced hepatic fibrosis	BMS-986263	2/1
	Non-alcoholic steatohepatitis	ARO-HSD	1/0
Viral			16/5
	RSV	ALN-RSV01	4/0
	Chronic HBV	ARC-520: 6/0	9/3
		JNJ-73763989: 2/0	
		JNJ-73763989 and JNJ-56136379: 1/0	
		RO7445482: 0/1	
		AB-729: 0/1	
		VIR-2218: 0/1	
	Ebola virus	TKM-13080	1/0
	HIV-1 infection	LVsh5/C46: 1/0	2/1
		HIV-shI-TAR-CCR5RZ: 1/0	
		CCR5 shRNA/TRIM5alpha/TAR decoy: 0/1	
	Coronavirus	MBS-COV	0/1
Kidney			6/5
	Primary Hyperoxaluria Type 1	Lumasiran: 4/4	5/5
		Nedosiran: 1/0	
		DCR-PHXC: 0/1	

	Acute Kidney Injury	Teprasiran	1/0
Eye			5/5
	wAMD	AGN-211745: 1/0	3/3
		PF-04523655: 2/0	
		OLX10212: 0/1	
		SYL1801: 0/1	
		4D-150: 0/1	
	DME	PF-04523655	1/0
	Elevated IOP associated to glaucoma	SYL040012	1/0
	Dry Eye Disease	Tivanisiran (SYL1001)	0/2
Blood			3/4
	Hemophelia A or B	Nedosiran: 1/0	1/1
		Fitusiran: 0/1	
	Sickle cell disease	BCH-BB694: 1/0	1/2
		CD34+ HSC-BCL11a: 0/2	
	Paroxysmal nocturnal hemoglobinuria	Cemdisiran	1/0
	Polycythemia Vera	SLN124	0/1
Skin			1/4
	Pachyonychia congenita	TD101	1/0
	Keloid	STP705	0/1
	Scar prevention	LEM-S401: 0/1	0/3
		BMT101: 0/1	
		OLX10010: 0/1	
Respiratory			2/0
	Alpha-1 antitrypsin deficiency	ARC-AAT	2/0
Gastrointestinal tract			1/0
	Chrons Disease	STNM01	1/0
Joint			0/1
	Gout	ALN-ZDH	0/1
Lipid-tissue			0/1
	Decrease inflammation to decrease abdominal obesity	STP705	0/1

Table S6: Tissue-targets of RNAi therapeutic. Diseases treated with RNAi therapeutics grouped by tissues targeted by the effector. Information regarding the name of the RNAi-based drug, the number of times the RNAi therapeutic has been used in published/ongoing clinical trials, and total number of diseases treated with RNAi therapeutic in published/ongoing clinical trials. The color of the boarder of the organ-boxes correlates with the color-coded annotations in Fig. 7 ASCVD, Atherosclerotic cardiovascular disease; hATTR, Hereditary ATTR amyloidosis; RSV, Respiratory Syncytial Virus; HBV, hepatitis B virus; HIV-1, Human Immunodeficiency Virus-1; wAMD, wet Age-dependent Macular Degeneration; DME, Diabetic Macular Edema; IOP, Intraocular Pressure.

Organ	Disease	Name of drug and how many (published/ongoing)	Number in total (published/ongoing)
Tumor			19/11
	Cancer with CNS involvement	ATN-RNA:1/0	2/0
		NU-0129: 1/0	
	Advanced cancer	FANG/VIGIL: 2/0	6/4
		Atu27:1/0	
		CALAA-01: 1/0	
		STMN1: 1/0	
		MRX34: 1/0	
		EphA2 siRNA: 0/1	
		NBF-006: 0/1	
		INT-1B3: 0/1	
		ALN-HSD: 0/1	
	Cancer with liver involvement	ALN-VSP: 2/0	3/0
		TKM-080301: 1/0	
	Recurrent Malignant Pleural Mesothelioma	TargomiR	1/0
	Central nervous system B-cell acute lymphocytic leukemia	ssCART-19s	1/0
	Cancer with pancreas involvement	siG12D-LODER: ½	2/2
		ATU027: 1/0	
	Relapsed or Refractory B-cell acute lymphoblastic leukemia	ssCAR-T19	1/0
	Acute leukemia	Ad-siSSF-DC	1/0
	Recurrent B-Cell Non-Hodgkin Lymphoma	CAS3/SS3	0/1

	Cancer with female reproductive organs involved	FANG/VIGIL: 2/1	2/1
	Squamous Cell Carcinoma	STP705	0/1
	Ewings Sarcoma	pbi-shRNA: 1/0	0/2
		Vigil: 1/0	
Liver			46/20
	hATTR	Patisiran: 6/1	10/2
		ALN-TTR01: 1/0	
		Revusiran: 2/0	
		Vutrisiran: 1/1	
	Hemophelia A or B	Nedosiran: 1/0	1/1
		Fitusiran: 0/1	
	Alpha-1 antitrypsin deficiency (AATD)	ARC-AAT	2/0
	Acute hepatic porphyrias	Givosiran	5/0
	Atherosclerotic cardiovascular disease (ASCVD) and hypercholesterolemia	Inclisiran	15/6
	Primary Hyperoxaluria Type 1	Lumasiran: 4/4	5/5
		Nedosiran: 1/0	
		Lumasiran: 4	
		DCR-PHXC: 0/1	
	Paroxysmal nocturnal hemoglobinuria	Cemdisiran	1/0
	Elevated Apolipoprotein A (cardiovascular disease)	Olpasiran: 3/0	4/1
		SLN360: 1/1	
	Advanced hepatic fibrosis	BMS-986263	2/1
	Non-alcoholic steatohepatitis	ARO-HSD	1/0
	Polycythemia Vera	SLN124	0/1
	Hypertension	ALN-AGT01	0/2
	Gout	ALN-ZDH	0/1
Viral			16/5
	RSV	ALN-RSV01	4/0
	Chronic HBV	ARC-520: 6/0	9/3
		JNJ-73763989: 2/0	

		JNJ-73763989 and JNJ-56136379: 1/0	
		RO7445482: 0/1	
		AB-729: 0/1	
		VIR-2218: 0/1	
	Ebola virus	TKM-13080	1/0
	HIV-1 infection	LVsh5/C46: 1/0	2/1
		HIV-shI-TAR-CCR5RZ: 1/0	
		CCR5/shRNA/TRIM5alpha/TAR decoy: 0/1	
	Coronavirus	MBS-COV	0/1
Kidney			1/0
	Acute Kidney Injury	Teprasiran	1/0
Eye			5/5
	Wet Age-dependent Macular Degeneration (wAMD)	AGN-211745: 1/0	3/3
		PF-04523655: 2/0	
		OLX10212: 0/1	
		SYL1801: 0/1	
		4D-150: 0/1	
	Diabetic Macular Edema (DME)	PF-04523655	1/0
	Elevated IOP associated to glaucoma	SYL040012	1/0
	Dry Eye Disease	Tivanisiran (SYL1001)	0/2
Blood			1/2
	Sickle cell disease	BCH-BB694: 1/0	1/2
		CD34+ HSC-BCL11a: 0/2	
Skin			1/4
	Pachyonychia congenita (PC)	TD101	1/0
	Keloid	STP705	0/1
	Scar prevention	LEM-S401: 0/1	0/3
		BMT101: 0/1	
		OLX10010: 0/1	
Gastrointestinal tract			1/0
	Chrons Disease	STNM01	1/0
Lipid-tissue			0/1
	Decrease inflammation to decrease abdominal obesity	STP705	0/1

Table S7: Approved RNAi therapeutics. Characteristics of five FDA and EMA approved RNAi-based drugs: Parisiran, Givosiran, Lumasiran, Inclisiran, Vutrisiran

	Patisiran	**Givosiran**	**Lumasiran**	**Inclisiran**	**Vutrisiran**
Year of approval by FDA and EMA	2018	2019	2020	2021	2022
Disease	Hereditary Transthyretin Amyloidosis (hATTR)	Acute Intermittent Porhyria	Primary Hyperox-aluria Type 1	Hypercholesterolaemia	hATTR
Delivery	Nanoparticle	Naked	Naked	Naked	Naked
Type of delivery	LNP	GalNAc conjugate	GalNAc conjugate	GalNAc conjugate	GalNAc conjugate
Type of RNAi	siRNA	siRNA	siRNA	siRNA	siRNA
Administration	Intravenous	Subcutaneous	Subcutaneous	Subcutaneous	Subcutaneous
Gene target	TTR	ALAS1	HAO1	PCSK9	TTR
Number of trials included in the published clinical trials	5	5	4	15	1
Number of trials included in the ongoing clinical trials	1	0	4	6	1

Table S8: PRISMA 2020 statement checklist.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 6 and Supplemental material
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary material
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6, Supplemental material
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6 and Supplemental material
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Supplemental material
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Supplemental material
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Not relevant
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6 and Supplemental

Section and Topic	Item #	Checklist item	Location where item is reported
			material
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Supplemental material
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6 and Supplemental material
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not relevant
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not relevant
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not relevant
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not relevant
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure S1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Not relevant
Study characteristics	17	Cite each included study and present its characteristics.	Not relevant
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Not relevant
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Not relevant
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not relevant
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not relevant
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not relevant
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not relevant
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not relevant
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not relevant
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 10-11
	23b	Discuss any limitations of the evidence included in the review.	Page 14
	23c	Discuss any limitations of the review processes used.	Page 14

Section and Topic	Item #	Checklist item	Location where item is reported
	23d	Discuss implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 5 and Supplemental material
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not relevant
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not relevant

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Table S9: Extraction protocol.

Variable	Categories	Definition of the variable
Article characteristics		
Title, Journal, Authors	**-**	Variables are filled out in spreadsheet automatically. **Important: Check that the variables correspond to the downloaded article to make sure you are extracting from the correct article.** The journal name for a specific journal may differ in the spreadsheet; should just be ignored. May be due to retrieval from different data bases (PubMed and Embase).
Name of last author	-	Enter full name
Name of first author	-	Enter full name
Year of publication	1998-2023	Years corresponding to search period. Choose year of reference publication **not epub** from drop down options.
Study setting (Country)	Categorical variable	Enter the English name of the country where the study was conducted (use this alphabetical list of countries; the spreadsheet should save the name of a country after first entry: https://www.worldometers.info/geography/alphabetical-list-of-countries/). Start with capital letter; make sure spelling is correct. The country should be selected based on the country corresponding to the last author´s affiliation.
Name of drug	-	Enter name

Disease	-	Enter disease
Target	Name of gene	E.g. "*TTR*" (https://www.genecards.org/cgi-bin/carddisp.pl?gene=TTR)
Delivery	Nanoparticle Naked Viral vector Other	
Type of delivery	Description of delivery platform	E.g. Lipid nanoparticle, Lentiviral vector, Cholesterol-conjugated
Type	siRNA miRNA shRNA miR-shRNA	
Administration	Description of administration route	E.g. Intravenous, Subcutaneous, Intranasal, Inhalation

Supplemental Document: The full search strategy. Included are inclusion/exclusion criteria for identification of published/ongoing clinical trials via databases and ClinicalTrials.gov.

Inclusion criteria:
Original research articles on RNA interference published between 1998-2023
Human *in vivo* clinical trials

Exclusion criteria:
Non-original articles
Articles published before Fire and Mello´s 1998-paper[2].
In vitro or *ex vivo* studies
No intervention

Search engines/databases (assessed December 30, 2022 (Web of Science, PubMed and Embase and January 18, 2023 (ClinicalTrials.gov)):
Web of Science (All Databases)
Assessed using Google Chrome Version 108.0.5359.124 (Official version) (arm64)
https://www.webofscience.com/wos/alldb/advanced-search

PubMed (assessed using Google Chrome Version 108.0.5359.124 (Official version) (arm64)
https://pubmed.ncbi.nlm.nih.gov

Embase (assessed using Google Chrome Version 108.0.5359.124 (Official version) (arm64)
https://www.embase.com/search/quick

ClinicalTrials.gov
Assessed using Google Chrome Version 108.0.5359.124 (Official version) (arm64)
https://clinicaltrials.gov

Web of Science search strategy (results: 1,016)
https://www.webofscience.com/wos/alldb/summary/1b1bdc88-e1ea-4f32-a752-b53bcd7631ba-67e7634c/times-cited-descending/1

(TI=("RNA interference" OR RNAi* OR "posttranscriptional gene silencing" OR "post-transcriptional gene silencing" OR "post transcriptional gene silencing" OR PTGS OR "RNA silencing" OR "small interfering RNA*" OR siRNA* OR "short hairpin RNA*" OR "small hairpin RNA*" OR shRNA* OR microRNA* OR miRNA*) OR AB=("RNA interference" OR RNAi* OR "posttranscriptional gene silencing" OR "post-transcriptional gene silencing" OR "post transcriptional gene silencing" OR PTGS OR "RNA silencing" OR "small interfering RNA*" OR siRNA* OR "short hairpin RNA*" OR "small hairpin RNA*" OR shRNA* OR microRNA* OR miRNA*))

Refined by:
Publication Years: 1998-2023

Document Types: Clinical Trial
NOT Document Types: Abstract OR Review Article OR Editorial Material

PubMed search strategy (results: 1,060)
("RNA interference"[Title/Abstract] OR RNAi*[Title/Abstract] OR "posttranscriptional gene silencing"[Title/Abstract] OR "post-transcriptional gene silencing"[Title/Abstract] OR "post transcriptional gene silencing"[Title/Abstract] OR PTGS[Title/Abstract] OR "RNA silencing"[Title/Abstract] OR "small interfering RNA*"[Title/Abstract] OR siRNA*[Title/Abstract] OR "short hairpin RNA*"[Title/Abstract] OR "small hairpin RNA*"[Title/Abstract] OR shRNA*[Title/Abstract] OR microRNA*[Title/Abstract] OR miRNA*[Title/Abstract]) AND ("1998/01/01"[Date - Publication] : "2023/12/31"[Date - Publication]) AND (clinicaltrial[Filter] OR clinicaltrialphasei[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR controlledclinicaltrial[Filter]) NOT ("review"[Publication Type] OR "editorial"[Publication Type])

Embase search strategy (results: 647)
('rna interference':ab,ti OR 'rnai*':ab,ti OR 'posttranscriptional gene silencing':ab,ti OR 'post-transcriptional gene silencing':ab,ti OR 'post transcriptional gene silencing':ab,ti OR 'ptgs':ab,ti OR 'rna silencing':ab,ti OR 'small interfering rna*':ab,ti OR 'sirna*':ab,ti OR 'short hairpin rna*':ab,ti OR 'small hairpin rna*':ab,ti OR 'shrna*':ab,ti OR 'microrna*':ab,ti OR 'mirna*':ab,ti) AND [01-01-1998]/sd NOT [31-12-2023]/sd AND ('clinical trial'/de OR 'controlled clinical trial'/de OR 'phase 1 clinical trial'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de) NOT ('conference abstract'/it OR 'conference paper'/it OR 'conference review'/it OR 'review'/it OR 'editorial'/it OR 'note'/it)

ClinicalTrials.gov search strategy (results: 450):
Other terms (Recruiting, Enrolling by invitation, Active, not recruiting): "RNA interference" OR RNAi OR "small interfering RNA" OR siRNA OR "short hairpin RNA" OR "small hairpin RNA" OR shRNA OR microRNA OR miRNA

References

1. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ *372*: n71.
2. Fire A, Xu S, Montgomery MK, Kostas SA, Driver SE, and Mello CC (1998). Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. Nature *391*: 806-811.