

Supplementary materials

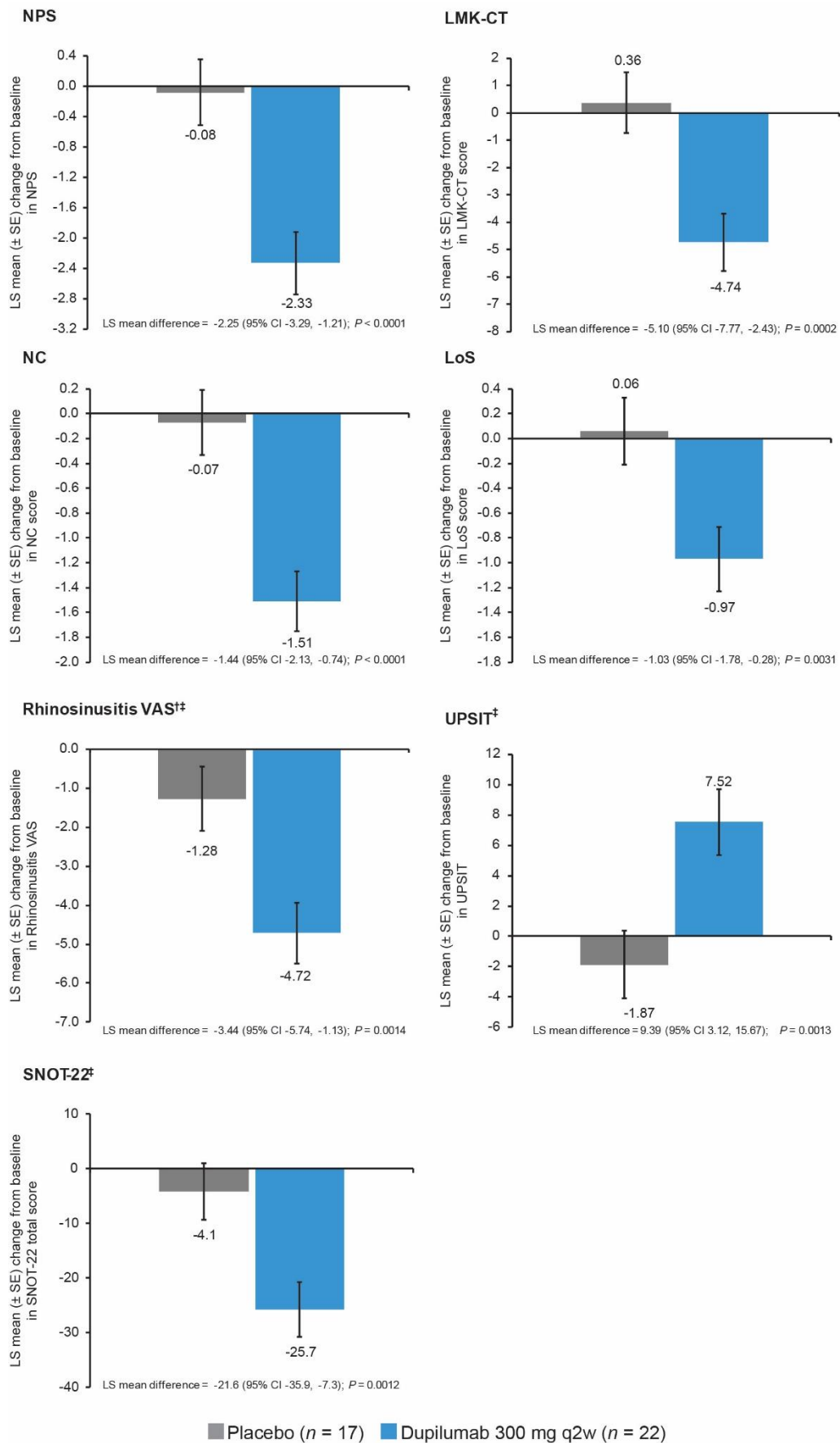


Figure S1. LS mean change from baseline in CRSwNP outcomes for placebo and dupilumab 300 mg q2w at week 52 (SINUS-52, subgroup of patients with NPS = 8)*

Each of the imputed complete data was analyzed by fitting an ANCOVA model with the corresponding baseline value, treatment group, asthma/NSAID-ERD status, prior NP surgery, and region as covariates. Analysis was based on the same imputed dataset using WOCF/MI from primary analysis of the coprimary endpoints

*PNIF data were not collected during the week 24 to week 52 period in SINUS-52

†Placebo $n = 16$, ‡Dupilumab $n = 21$

NPS: nasal polyp score; LS: least squares; SE: standard error; CI: confidence interval; LMK-CT: Lund-Mackay computed tomography; NC: nasal congestion/obstruction; LoS: loss of smell; VAS: visual analog scale; UPSIT: University of Pennsylvania Smell Identification Test; SNOT-22: 22-item Sinonasal Outcome Test; q2w: every 2 weeks; CRSwNP: chronic rhinosinusitis with nasal polyps; ANCOVA: analysis of covariance; NSAID-ERD: nonsteroidal anti-inflammatory drug-exacerbated respiratory disease; NP: nasal polyps; WOCF: worst observation carried forward; MI: multiple imputation; PNIF: peak nasal inspiratory flow

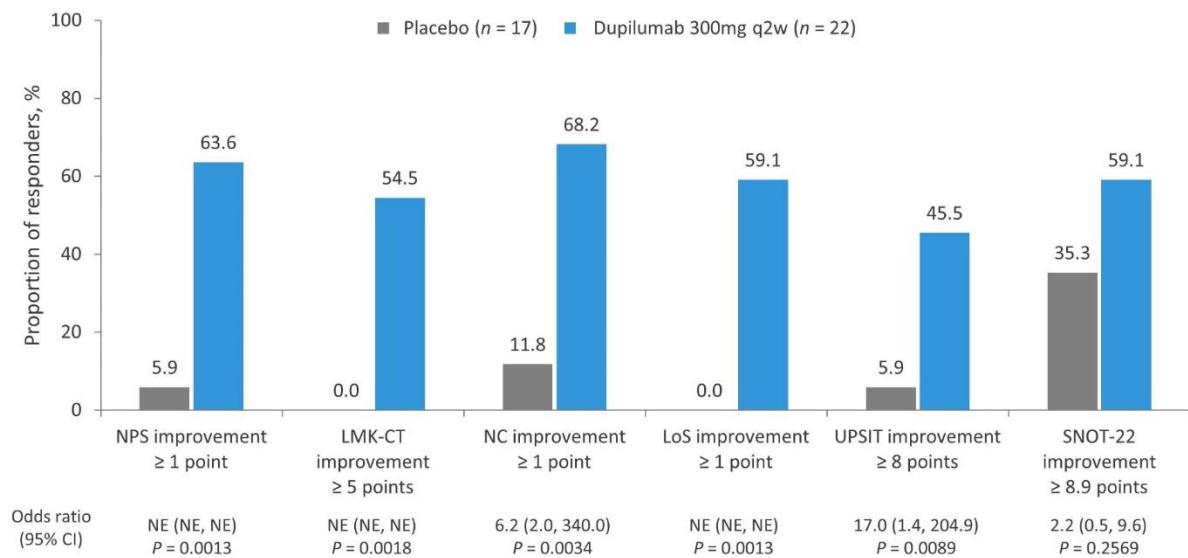


Figure S2. Proportion of responders for placebo and dupilumab 300 mg q2w at week 52 (SINUS-52, subgroup of patients with NPS = 8)*

Odds ratios were derived from the Mantel-Haenszel estimator, with Cochran-Mantel-Haenszel test performed on the association between the responder status and treatment group (dupilumab vs. placebo), stratified by asthma/NSAID-ERD status, prior surgery history, and region

*PNIF data were not collected during the week 24 to week 52 period in SINUS-52

q2w: every 2 weeks; NPS: nasal polyp score; LMK-CT: Lund-Mackay computed tomography; NC: nasal congestion/obstruction; LoS: loss of smell; UPSIT: University of Pennsylvania Smell Identification Test; SNOT-22: 22-item Sinonasal Outcome Test; CI: confidence interval; NE: not evaluable; NSAID-ERD: nonsteroidal anti-inflammatory drug-exacerbated respiratory disease; PNIF: peak nasal inspiratory flow

Table S1. List of Institutional Review Boards and Independent Ethics Committees for SINUS-24 and SINUS-52

SINUS-24

Bulgaria	Ethics Committee Multicenter Trials, 5 Sveta Nedelya Square, Sofia 1000
Czech Republic	Eticka Komise Fakultni Nemocnice Hradec Kralove Sokolska 581, Hradec Kralove 500 05
France	CPP Sud-Méditerranée 4 Centre Hôpitalier Universitaire de Montpellier Hôpital Saint Eloi 2, Avenue Bertin Sans Montpellier Cedex 05 34295
Germany	Ethik-Kommission des Landes Berlin, Landesamt für Gesundheit und Soziales Berlin Geschäftsstelle der Ethik-Kommission des Landes Berlin, Fehrbelliner Platz 1, Berlin 10707
Hungary	Egészségügyi Tudományos Tanács, Klinikai Farmakológiai Etikai Bizottsága, Arany János út 6-8 Budapest 1051
Italy	Area Vasta Nord Ovest AOUP Comitato per la Sperimentazione Clinica dei Medicinali, Via Roma 67, Pisa 56126, Pisa
	AOU Policlinico-Vittorio, Emanuele, Via S. Sofia 78 Comitato Etico Catania 1, Catania 95123, Catania
	Ospedale di Circolo e Fondazione Macchi, Comitato Etico, Viale Luigi Borri 57, Varese, 21100, Varese
	Ospedale San Raffaele, Via Olgettina 60, Comitato Etico, Milano, 20132, Milano
	Istituto Clinico Humanitas, Comitato Etico dell'IRCCS, Istituto Clinico Humanitas di Rozzano (MI), Via Manzoni 56, Rozzano 20089, Milano
	Comitato Etico dell'A.O. San, Paolo, Via Di Rudini 8, Milano 20142, Milano
	Comitato Etico Interaziendale, Bologna-Imola, Comitato Etico Interaziendale, Bologna-Imola, Via Castiglione 29, Bologna, 40124, Bologna
Netherlands	Medisch Ethische Toetsingscommissie Academisch, Medisch Centrum Meibergdreef 9, Amsterdam 1105 AZ
Poland	Komisja Bioetyczna przy Uniwersytecie Medycznym w Lodzi, Pl Hallera 1B Lodz 90-647, Łódzkie
Romania	Nat Bioethics Committee of Medical Product – Medical Devices, 19-21 Stefan Cel Mare Street, District 2, Bucharest 020125
Russian Federation	Ethics Board at Ministry of Health of the Russian Federation, 3, Rakhmanovskiy per., Moscow, 127994
	LEC of the “Alliance, Biomedical – Russian, Group”, LLC, 126, Griboedov canal emb., Saint-Petersburg, 190068

	LEC of Saint-Petersburg, Research Institute of ENT, and Speech, 9, Bronnitskaya str., Saint-Petersburg, 190013
	LEC of the Federal State, Institution "Polyclinic #3", 31 Grokholsky per., Moscow, 129090
	LEC of the 1st Moscow State, Medical University n.a., Sechenov, 8/2 Trubetskaya str., Moscow, 119991
	LEC of the Clinical, Emergency Hospital, n.a.N.V.Solovyov, 11, Zagorodny Sad str., Yaroslavl' Russia, 150003, Yaroslavl', 150003, Russia
	LEC of St Petersburg State, Medical University n.a., Pavlov, 10 Rentgena str., St Petersburg, 197101
Ukraine	LEC of Poltava Regional, Clinical Hospital n.a., Sklyfosofsky, 23 Shevchenko Str., Poltava, 36011
	LEC of the Central City, Clinical Hospital, 114, Hetmana Mazepy Str., Ivano-Frankivsk, 76000
	LEC of the Regional Clinical, Center of Radiation, Protection, 85 Novgorodska, Str., Kharkiv, 61166
	LEC of the Main Military, Medical Clinical Center, CMCH of MD, 18 Hospitalna Str., Kyiv, 01133
	LEC of the Institute of Otolaryngology n.a. Prof. O.S., Kolom, 3 Zoologichna Str., Kyiv, 03680
	LEC of Ternopil Municipal, City Hospital №2, 14 Kupchynskogo Str., Ternopil, 46000
United Kingdom	Tayside Medical Science Centre, Residency Block, Level 3, Ninewells Hospital & Medical School, George Pirie Way, Dundee, DD1 9SY
United States	Copernicus Group IRB, 5000 CentreGreen Way, Suite 200, Cary, 27513, NC
	Copernicus Group IRB, One Triangle Drive, Suite 100, Durham, 27713, NC
	Vanderbilt University IRB, 1313 21st Ave. S, Rm., 504 Oxford House, Nashville, 37232, TN
	Mayo Clinic IRB, 200 First Street SW, 201 Bldg. Room 4-60, Rochester, 55905, MN
	Western Institutional Review Board, 1019 39th Avenue SE, Suite 120, Puyallup, 98374-2115, WA
	Medical College of Wisconsin/Froedtert Hospital, 8701 Watertown Plank Road, PO Box 26509, Milwaukee, 53226, WI

	Chesapeake Research, Review IRB, 6940 Columbia Gateway Drive, Suite 110, Columbia, 21046, MD
	Office of Research Integrity, Medical University of SC, 19 Hagood Avenue, Room 601, P.O. Box 250857, Charleston, 29425, SC

SINUS-52

Argentina	Comite de Etica en, Investigacion INAER, Arenales 3146 1A, Caba C1425BEN, Buenos Aires
	Investigaciones en Alergia y, Enfermedades Respiratorias, Arenales 3146 1B, Caba C1425BEN, Buenos Aires
	Comite de Etica en, Farmacologia Clinica, Paraguay 2041 9no H, Caba C1121ABE, Buenos Aires
	Centro Medico de Enfermedades Respiratorias Esmeralda 1550, Vicente López B1602DQD, Buenos Aires Province
	Comite Independiente de Etica para Ensayos en Farm. Clínica, Av. Cabildo 1536 5°B Caba C1426ABP, Buenos Aires
	Comite de Etica Dr. Claude Bernard, San Lorenzo 2555 Rosario S2000KPG, Santa Fe
Australia	The Alfred Research & Ethics Unit, Commercial Road, Prahran 3181, Victoria
	Monash Health Human Research Ethics Committee 246, Clayton Road, Clayton 3168, Victoria
	Bellberry Limited, 129 Glen Osmond Road, Eastwood 5063, South Australia
Belgium	UZ Gent, Corneel Heymanslaan 10 Dienst Neus-Keel en Oorheelkunde, Gent 9000
Canada	The University of British Columbia Office of Research Ethics, Clinical Research Ethics Board, Room 210, 828 West 10th Avenue, Vancouver V5Z 1L8, BC
	Comite d'ethique de la recherche du CHUM, 900 rue St-Denis, Pavillon R, R03.456, Montreal H2X 0A9, QC
	Institutional Review Board Services (IRB Services) 372 Hollandview Trail, Suite 300, Aurora L4G 0A5, ON
	Queen's University Health Sciences REB, Office of Research Services Fleming Hall/Jemmett Wing Kingston, K7L 3N6, ON
Chile	Comite de Etica de la Investigacion S.S.M Sur Oriente, Av. Concha y Toro #3459 Puente Alto, Santiago 8207257, RM Region Metropolitan

	Comité de Ética Científico, S.S. M Oriente, Av. Salvador #364 Providencia Santiago, 7500922, RM Region Metropolitan
Israel	Ethics Committee of Hillel Yaffe Medical Center, EC of Hillel Yaffe MC PO Box 169, Hadera 38100
	Ethics Committee of Rabin Medical Center, EC of Rabin Medical Center 39 Jabotinsky Street, Petach Tikva 49100
	Galilee Medical Center Helsinki Committee of Galilee Medical Center, Nahariya 22100
	Ethics Committee of Kaplan Medical Center, EC of Kaplan MC, PO Box 1 Rehovot 76100
Japan	JCHO Shimonoseki Medical Center Institutional Review Board, 3-3-8 Kamishinchi-cho Shimonoseki-Shi 750-0061, Yamaguchi
	Shin Nihonbashi Ishii Clinic Institutional Review Board Kobunacho 8-6 Sinedobashi Bld.3kai, Nihombashi, Chuo-Ku 103-0024, Tokyo
	Japanese Red Cross Kyoto Daini Hospital IRB, 355-5 Haruobi-cho Kamanzadori Kamigyo-ku, Kyoto-Shi 602-8026, Kyoto
	Institutional Review Board of Nippon Medical School Hospital, 1-1-5 Sendagi Bunkyo-Ku 113-8062, Tokyo
	Institutional Review Board of KKR Tohoku Kosai Hospital 2-3-11 Kokubuncho, Aoba-ku Sendai-Shi 980-0803, Miyagi
	Shinagawa East One Medical Clinic, 2-16-1 Konan Minato-Ku 108-0075, Tokyo
	Human Rights and Ethics for Clinical Studies IRB, 13-2, Ichiban-cho Chiyoda-Ku 102-0082, Tokyo
	Institutional Review Board of the University of Tokyo Hospital 7-3-1 Hongo, Bunkyo-Ku 113-8655, Tokyo
	Institutional Review Board of Kansai Medical University Hospital 2-3-1, Shin-machi Hirakata-Shi 573-1191
	Institutional Review Board of Hiroshima University Hospital 1-2-3, Kasumi, Minami-ku Hiroshima-Shi 734-8551, Hiroshima
	Nihon University Hospitals' Joint Institutional Review Board, 30-1 Oyaguchi Kami-cho Itabashi-Ku 173-8610, Tokyo
	IRB of Kansai Medical University Medical Center 10-15, Fumizonochi Moriguchi-Shi 570-8507, Osaka
Rinku General Medical Center Institutional Review Board, 2-23 Rinkuourakita Izumisano-Shi 598-8577, Osaka	

	IRB of Nippon Medical School Chiba Hokusoh Hospital, 1715 Kamagari Inzai-Shi 270-1694, Chiba
	Nippon Medical School Musashikosugi Hospital IRB 1-396 Kosugi-cho, Nakahara-ku, Kawasaki-Shi 211-8533, Kanagawa
	IRB of Toho University Omori Medical Center, 6-11-1, Omorinishi Ota-Ku 143-8541
	Institutional Review Board of Otemae Hospital, 1-5-34 Otemae, Chuo-ku Osaka-Shi 540-0008, Osaka
	Institutional Review Board of University of Fukui Hospital 23-3 Matsuokashimoaizuki, Eiheiji-cho Yoshida-Gun 910-1193, Fukui
	Kitakyusyu Municipal Medical Center IRB, 2-1-1 Basyaku, Kokurakita-ku Kitakyushu-Shi 802-0077, Fukuoka
	IRB of Tohoku Medical & Pharmaceutical University Hospital, 1-12-1 Fukumuro Miyagino-ku, Sendai-Shi 983-8512, Miyagi
	Institutional Review Board of Tokyo Kyosai Hospital, 2-3-8 Nakameguro Meguro-Ku 153-8934, Tokyo
	IRB of Hoshikuma Dermatology Allergy Clinic 2-1-1 Noke, Sawara-ku Fukuoka-Shi 814-0171, Fukuoka
	Institutional Review Board of Okayama University Hospital 2-5-1 Shikata-cho, Kita-ku Okayama-Shi 700-8558, Okayama
	Institutional Review Board of Juntendo University Hospital 3-1-3 Hongo, Bunkyo-Ku 113-8431, Tokyo
	Institutional Review Board of JCHO Kyushu Hospital, 1-8-1 Kishinoura, Yahatanishi-ku Kitakyushu-Shi 806-8501, Fukuoka
	Institutional Review Board of Osaka Medical College Hospital, 2-7, Daigakumachi Takatsuki-Shi 569-8686, Osaka
	Sugiura Clinic Institutional Review Board, 4-4-16-301 Honcho Kawaguchi-Shi 332-0012, Saitama
	Tokyo-Eki Center-building Clinic Institutional Review Board, 3-3-14 Nihombashi Chuo-Ku 103-0027, Tokyo
Mexico	CEI Hospital Christus Muguerza del Parque S.A de C.V. Chih. Dr. Pedro Leal Rodriguez No. 1802 Col. Centro, Chihuahua 31000, Chihuahua
	CEI Centro Hospitalario Vicor, Nebulosa No. 2956 Col. Jardines del Bosque, Guadalajara 44520, Jalisco
	CI Instituto Jalisciense de Investigacion Clinica S.A de C.V, Penitenciaría No. 20. Col. Centro, Guadalajara 44100, Jalisco

	CEI de la Facultad de Medicina y HU de la UANL Av. Francisco I. Madero y Gonzalitos V S/N Col. Mitras Centro, Monterrey 64460
	CI de la Facultad de Medicina y HU de la UANL Av. Francisco I. Madero y Gonzalitos S/N Col. Mitras Centro, CI del Hospital Universitario Dr. José Eleuterio Gonzalez, Monterrey 64460, Nuevo Leon
	CEI Hospital Angeles Chihuahua, Calle Haciendas del Valle No. 7120, Col. Plaza Las Haciendas, Chihuahua 31238, Chihuahua
Portugal	CEIC – Comissão de Ética para a Investigação Clínica Parque da Saúde de Lisboa, Pav. 17-A, Avenida do Brasil nº 53, Lisboa 1749-004
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	LEC of St Petersburg State Medical University n.a. Pavlov 10, Rentgena str. St Petersburg 197101
	LEC of the “Alliance Biomedical – Russian Group”, LLC 126, Griboedov canal emb., Saint-Petersburg, 190068
	LEC of Stavropol Regional Clinical Hospital, 1, Semashko str. Stavropol 355030
	LEC of Clinical Research Centre for Otorhinolaryngology 30/2, Volokolamskoe Shosse, Moscow 123182
Spain	Hospital Clinic i Provincial Villarroel, 170 Barcelona 08036, Barcelona
Sweden	Regionala etikprövningsnämnden i Stockholm, Regionala etikprövningsnämnden FE 289, Stockholm 171 77
Turkey	Istanbul Universitesi Tıp Fakultesi Yerel Etik Kurulu Istanbul Universitesi Istanbul Tıp Fakultesi, Tıbbi Arastirmalar Yerel Etik Kurulu, Capa Istanbul 34000
	Türkiye İlaç ve Tıbbi Cihaz Kurumu, Sogutozu mah. 2176 sok no: 5, Cankaya-Ankara 06520
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	University of Utah IRB 75 S 2000 East, RAB 111, Salt Lake City 84112, UT
	Yale University Health Investigation Committee, 25 Science Park, 3rd Floor, 150 Munson St., New Haven 06520, CT
	Brany IRB, 1981 Marcus Ave., Suite 210, Lake Success 11042, NY

IRB: Institutional Review Board