**Supplementary Table 1:** IRB/IEC centers for the WISDOM study by country

| **Country** | **IRB/IEC centres** |
| --- | --- |
| Australia | * Sydney South West Area Health Service Research Development Office, Level 3 Building 92 Royal Prince Alfred Hospital Camperdown NSW 2050 Australia * Bellberry Human Research Ethics Committee 229 Greenhill Road Dulwich South Australia 5065 Australia * Repatriation General Hospital Research and Ethics Committee Daws Road, Daw Park South Australia 5041 Australia. Changed to: Southern Adelaide Health Service/Flinders University Human Res. Ethics Committee * Ethics of Human Research Committee (TQEH & LMH) The Queen Elizabeth Hospital 28 Woodville Road Woodville South Australia 5011 & Lyell McEwin Hospital Haydown Road Elizabeth Vale, South Australia 5112 Australia |
| Belgium | * Commissie Medische Ethiek UZ KU Leuven/ Campus Gasthuisberg Herestraat 49 3000 Leuven * Comitê de Ética em Pesquisa da Pontifícia Universidade Católica do Rio Grande do Sul Av. Ipiranga 6690 3º andar - Sala 314 CEP: 90610-000 Porto Alegre – RS * Comitê de Ética em Pesquisa do Hospital Geral de Goiânia Av. Anhanguera, 6479 Setor Oeste –CEP: 74110-010 Goiânia/GO |
| Brazil | * Comitê de Ética em Pesquisa da Universidade Federal de São Paulo/ Hospital São Paulo, Rua Botucatu, 572 1º andar conjunto 14 CEP: 04023-062 São Paulo – SP * Comitê de ética em Pesquisa do Hospital das Clínicas da Universidade Federal de Goiás, 1ª Avenida, s/n - Setor Leste Universitário CEP: 74.605-050 Goiânia – GO * Comitê de Ética em Pesquisa em Seres Humanos da Irmandade da Santa Casa de Misericórdia de Porto Alegre R. Prof. Annes Dias, 295 CEP: 90020-090 Porto Alegre – RS |
| Bulgaria | * Ethics Committee for Multicentre Trials 26 Yanko Sakazov blvd. * Ethics Committee for Multicentre Trials 8 Damyan Gruev str. * Ethics Committee for Multicentre Trials Sofia 5, Sveta Nedelya square |
| China | * IRB of The First Affiliated Hospital of Guangzhou Medical College, No.151 Yanjiang Road, Guangzhou, Guangdong Province, China, 510120 * IRB of Peking University Third Hospital, No.49 North Huayuan Road, Haidian, District. Beijing, China, 100083 * IRB of Beijing Chao Yang Hospital Affiliate of Capital University of Medical School, No.8, Gongtinan Road, Chaoyang, District, Beijing, China, 100120 * IRB of Zhongshan Hospital Fudan University, No.180 Fenglin Road, Shanghai, China, 200032 * IRB of Shanghai Pulmonary Hospital No.507 Zhengmin Road, Shanghai, China, 200433 * IRB of Peking Union Medical College Hospital, No.1 Shuaifu Yuan Street, Wangfujing, Beijing, China, 100730 * IRB of Union Hospital, Tongji Medical College of Huazhong University of Science & Technology No.1277 Jiefang Avenue, Hankou District, Wuhan, Hubei Province, China, 430022 * IRB of The First Affiliated Hospital, Chongqing Medical University, No.1 Youyi Rd. Yuzhong District, Chongqing, China, 400016 |
| Denmark | * Den Videnskabsetiske Komité for Region Midtjylland Sundhedssekretariatet Skottenborg 26, Postboks 21 8800 Viborg |
| France | * CPP Sud Méditerranée II Hôpital Salvator 249 Boulevard Sainte Marguerite 13274 MARSEILLE Cedex 09 |
| Germany | * Ethik-Kommission der Ärztekammer Schleswig-HolsteinBismarckallee 8-12 23795 Bad Segeberg * Ethik-Kommission an der Universität Regensburg Franz-Josef-Strauß- Allee 11 93042 Regensburg * Ethik-Kommission der Medizinischen Fakultät der Universität zu Köln Forum/Gebäude 42 Joseph-Stelzmann-Str. 20 50931 Köln * Ethik-Kommission der Landesärztekammer Rheinland-Pfalz Deutschhausplatz 3, 55116 Mainz * Kommission für Ethik in der ärztlichen Forschung des Fachbereichs Humanmedizin der Philipps-Universität Marburg Baldingerstraße 1 35043 Marburg * Ethik-Kommission der Medizinischen Fakultät Heidelberg, Alte Glockengießerei 11/1 69115 Heidelberg * Ethikkommission der Medizinischen Fakultät der Ruhr-Universität Bochum, BG-Kliniken Bergmannsheil Bürkle-de-la-Camp- Platz 1 44789 Bochum * Sächsische Landesärztekammer Schützenhöhe 16 01099 Dresden * Landesamt für Gesundheit und Soziales Berlin Geschäftsstelle der Ethik-Kommission des Landes Berlin Fehrbelliner Platz 1 10707 Berlin * Ethik-Kommission der Landesärztekammer in Hessen Im Vogelsgesang 3 60488 Frankfurt * Ethik-Kommission der Medizinischen Fakultät der LMU Marchioninistr. 15   81377 München   * Ethik-Kommission der Medizinischen Fakultät der Christian-Albrechts-Universität zu Kiel Arnold-Helle-Straße 3 Haus 9 24105 Kiel * Ethik-Kommission der Landesärztekammer Brandenburg Dreifertstr. 12 03044 Cottbus |
| Greece | * EED Leoforos Mesogion 284, P.C: 15562 Cholargos Athens * OF Leoforos Mesogion 284, P.C: 15562 Cholargos Athens * EOF Leoforos Mesogion 284, P.C: 15562 Cholargos Athens |
| Hungary | * CEC: Medical Research Council Ethics Committee for Clinical Pharmacology 1051Budapest Arany János utca * Réthy Pál Kórház Intézeti Kutatásetikai Bizottság 5600 Békéscsaba Gyulai utca 18 * Szegedi Egyetem ÁOK Intézeti Kutatásetikai Bizottság 6701 Szeged Korányi Fasor 8-10 * Intézeti Kutatásetikai Bizottság Toldy Ferenc Kórház 2700 Cegléd Gubody u 3/A * Selye János Kórház Rendelőintézet Intézeti Kutatásetikai Bizottság 2900 Komárom, Széchenyi út 2 * Intézeti Kutatásetikai Bizottság Pest Megyei Tüdőgyógyintézet 2045 Törökbálint Munkácsy Mihály utca 40 * Intézeti Kutatásetikai Bizottság Mohácsi Kórház 7700 Mohács Szepesi tér 7 * Intézeti Kutatásetikai Bizottság Fejér Megyei Szent György Kórház 8000-Székesfehérvár Seregélyesi út 3 * Intézeti Kutatásetikai Bizottság Veszprém Megyei Tüdőgyógyintézet 8582 Farkasgyepű Somlóvári út * Karolina Kórház Rendelőintézet Intézeti Kutatásetikai Bizottság 9200 Mosonmagyaróvár Régi Vámház tér 2-4 * Sopron Erzsébet Oktató Kórház Intézeti Kutatásetikai Bizottság 9400 Sopron Győri utca 2. * Intézeti Kutatásetikai Bizottság Pest Megyei Tüdőgyógyintézet 2045 Törökbálint Munkácsy Mihály utca 40 |
| Italy | * Comitato per la sperimentazione clinica dei medicinali Azienda Ospedaliero- Universitaria Pisana Via Roma 67 56126 PISA * (OLD IRB IEC) Comitato Etico dell’Azienda Ospedaliera Garibaldi – S. Luigi-Currò – Ascoli- Tomaselli di Catania P.zza S.M. Gesu´, 7 95125 Catania * (NEW IRB IEC) Comitato Bioetico dell’Azienda Ospedaliera Universitaria Policlinico Vittorio Emanuele di Catania Via Santa Sofia, 78 95123 CATANIA * Comitato Etico Provinciale di Modena Via de Pozzo 71 41100 MODENA * Comitato Etico Azienda Ospedaliera Istituti Clinici di Perfezionamento Via Castelvetro, 32 201540 MILANO * Comitato Etico Azienda Ospedaliero Universitaria Ospedali Riuniti Foggia Viale Luigi Pinto 71100 FOGGIA * Comitato Etico Centrale dell’IRCCS Fondazione Salvatore Maugeri di Pavia Via Salvatore Maugeri, 4 27100 PAVIA * Comitato Etico Provinciale c/o Azienda Ospedaliero Universitaria di Ferrara Via Aldo Moro, 8 44124 Cona (FE) |
| The Netherlands | * Central IRB/IEC: METC Atrium Orbis Zuyd Postbus 4446 6401 CX Heerlen |
| New Zealand | * Multi-region Ethics Committee Ministry of Health No 1 The Terrace PO Box 5013, Wellington 6145 * Changed name to: Health and Disability Ethics Committee Ministry of Health No 1 The Terrace PO Box 5013 Wellington 6145 |
| Philippines | * MCU- Filemon Dionisio Tanchoco Medical Foundation, Epifanio Delos Santos Avenue, Caloocan City, 1400 * University of the Philippines Manila Research Ethics Board 2/F Paz Mendoza Building, College of Medicine, UP , Manila 547 Pedro Gil St., Ermita, Manila, 1000 * Manila Doctors Hospital. U.N. Avenue, Ermita Manila 1000 * Philippine Heart Center Institutional Ethics Review Board 8/F Medical Arts Building East Avenue, Quezon City,1100 * National Kidney Transplant Institute, East Avenue, Diliman Avenue, Quezon City, 1100 * FEU-NRMF Medical Center, Regalado Ave. Cor Dahlia St. West Fairview, Quezon City * Quirino Memorial Medical Center Hospital Ethics Committee Katipunan Rd corner P. Tuazon St. Project 4, Quezon City * Asian Hospital & Medical Center Institutional Review Board 2205 Civic Drive Filinvest Corporate City, Muntinlupa |
| Poland | * Komisja Bioetyczna przy Uniwersytecie Medycznymim. Karola Marcinkowskiego w Poznaniuul. Fredry 10 61-701 Poznań * Komisja Bioetyczna przy Okręgowej Radzie Lekarskiej Wielkopolskiej Izby Lekarskiej ul. Nowowiejskiego 51 61-734 Poznań * Komisja Bioetyczna przy Instytucie Gruźlicy i Chorób Płuc ul.Płocka 26 01-138 Warszawa * Komisja Bioetyczna Śląskiej Izby Lekarskiej w Katowicach ul. Grażyńskiego 49a 40-126 Katowice * Komisja Bioetyczna przy Dolnośląskiej Radzie Lekarskiej ul. Jana Matejki 6 50-333 Wrocław * Komisja Bioetyczna przy Okręgowej Izbie Lekarskiej ul. Reformacka 10 35-026 Rzeszów * Komisja Bioetyczna Śląskiej Izby Lekarskiej w Katowicach ul. Grażyńskiego 49a 40-126 Katowice |
| Russia | * Independent ethics committee of Saint Petersburg medical university n.a. Pavlov 197101, Saint Peterburg, Rentgena str, 10 * Independent bioethics committee of State Educational Institution of High Professional Education Samara State Medical University of Roszdrav Chapaevskaya str., 89, Samara, 443099, Russia * Local ethics committee of GBOU VPO “Saratov state medical university n.a. V.I. Razumovskii” 410054, Saratov, B. Sadovaya str., 137 * IEC of Municipal Institution of Healthcare” Yaroslavl Clinical hospital №8 ” Suzdalskoye shosse,39,150030, Yaroslavl, Russia * IEC of State Educational Institution of High Professional Education "Ivanovo State Medical Academy of Roszdrav" Fridrikha Engelsa pr., 8, 153012, Ivanovo, Ivanovskaya region, Russia * IEC of Federal State Institution “Outpatient Clinic # 3” of Russian Federation President’s Management Department Grokholski pereulok,31, 129090, Moscow, Russia * Local ethics committee of Ural state medical university 620028, Ekaterinburg, Repina str., 3 |
| South Africa | * University of Cape Town, Research Ethics Committee, Room E52-24, Groote Schuur Hospital, Observatory 7925, South Africa * Stellenbosch University, Committee for Clinical Trials, PO Box 19063, Tygerberg 7505, South Africa * Pharma Ethics (Pty) Ltd. 123 Amcor Road, Lyttelton Manor 0157, Irene, South Africa |
| Spain | * Comité Ético de Investigación Clínica de Euskadi (CEIC-E) Dirección de Farmacia Dpto. de Salud del Gobierno Vasco C/ Donostia-San Sebastian nº 1 01010 Vitoria-Gasteiz Spain |
| Taiwan | * Joint Institutional Review Board No. 201, sec. 2, Shih-pai Road,Taipei, Taiwan * Institutional Review Board of Tri-Service General Hospital No. 325, sec. 2, Cheng- Kung Road, Taipei, Taiwan * Research Ethics Committee of National Taiwan University Hospital No. 7, Chung-Shan South Road, Taipei, Taiwan * Joint Institutional Review Board No. 201, sec. 2, Shih- pai Road, Taipei, Taiwan / Institutional Review Board of Cheng Ching Hospital Taichung No. 118, Sec. 3, Chung-Kang Road, Taichung, Taiwan * Joint Institutional Review Board No. 201, sec. 2, Shih- pai Road, Taipei, Taiwan / Institutional Review Board of Kaohsiung Medical University Chung-Ho Memorial Hospital No. 100, Tz-You 1st Road, Kaohsiung, Taiwan * Institutional Review Board of Chung-Shan Medical University Hospital No. 110, Sec. 1, Chien- Kuo North Road, Taichung, Taiwan * Institutional Review Board of China Medical University Hospital No. 2, Yuh-Der Road, Taichung, Taiwan |
| Tunisia | * Comité d’éthique CHU Abderrahman Mami 2080 Ariana * Comité d’éthique EPS Charles Nicolle Bd du 9 Avril 1006 Tunis * Comité d’éthique CHU Farhet Hached Av Ibn Jazzar 4000 Souss * Comité d’éthique CHU Hedi ChakerAv Majida Boulila 3029 Sfax |
| Turkey | * T.C. Rector of Mersin University Faculty of Medicine * T.C. Rector of Ondokuz Mayıs University Medical Research Local Ethics Committee * Local Ethics Committee of Medical Faculty, Marmara University * Ethics Committee of Yedikule Chest Diseases and Chest Surgery Training and Research Hospital * Ethics Committee of Medical Faculty, Kocaeli University * Local Ethics Committee of Dr. Lütfi Kırdar Training and Research Hospital * T.C. Rector of Erciyes University Faculty of Medicine Local Ethics Committee * Ethics Committee of Yedikule Chest Diseases and Chest Surgery Training and Research Hospital * Ethics Committee of Ataturk University Chest Diseases and Chest Surgery Training and Research Hospital * Rector of Pamukkale University Faculty of Medicine Local Ethics Committee * Research Ethics Committee of Medical Faculty, Ege University * Ethics Committee of Sisli Etfal Training and Research Hospital * Ethics Committee of Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital * Research Ethics Committee of Medical Faculty, Uludag University * Research Ethics Committee of Medical Faculty, Ege University (Coordinator Ethics Committee) * Ethics Committee of Yedikule Chest Diseases and Chest Surgery Training and Research Hospital (Local Ethics Committee) |
| Ukraine | * Local Ethics Committee of the Ukrainian State Scientific Research Institute of Invalid Rehabilitation, Ministry of Health of Ukraine/ 104, Khmelnytske Shose, 21029, Vinnytsia, Ukraine * Local Ethics Committee of the City Clinical Hospital #13/ 137, Gagarina Ave. , Kharkiv, 61035, Ukraine * Ethics commission by Medical-sanitory department of Public Joint Stock ”Kharkiv tractor factory named after C. Ordzhonikidze”/ Moskovskiy pr-t, 275, Kharkiv, 61106, Ukraine * Local Ethics Committee of F.G. Yanovskyy Institute of Phthisiology and Pulmonology of AMS of Ukraine/10, Amosova Str., Kyiv, 03680, Ukraine * Local Ethics Committee of the City Clinical Hospital №1/ 96, Khmelnytske Shose, 21029, Vinnytsia, Ukraine * Local Committee of bioethics of the Regional center of Phtysiology and Pulmonology/ 17, Ivana-Franka str, Ivano-Frankivsk, 76018, Ukraine * Central Ethics Committee MOH of Ukraine * State Expert Center MOH of Ukraine 03151, Kiev, Ukraine, Ushynskogo str., 40 |
| United Kingdom | * Leicestershire, Northamptonshire & Rutland REC 2, 1 Standard Court, Park Row, Nottingham, NG1 6GN * NRES Committee East Midlands – Norththampton, The Old Chapel Royal Standard Place Nottingham NG1 6FS |

**Supplementary Figure 1**: Percentage of patients with at least one moderate or severe exacerbation with ICS withdrawal in (A) patients taking triple therapy at screening and (B) the overall trial population

**Notes:** The numbers above the bars indicate percentages of patients with at least one exacerbation during the time periods (x axis)

\*Indicates the ratio of the percentages of patients with at least one exacerbation within the ICS continuation and ICS withdrawal groups

Percent of patient with first exacerbation per window is calculated as 100\*(number of patients with first exacerbation)/(number of patients at risk)

Percent of patient with exacerbation (including all unique exacerbations) per window is calculated as 100\*(number of patients with exacerbation)/(number of patients treated)

**Abbreviations:** exc, exacerbations;ICS, inhaled corticosteroid