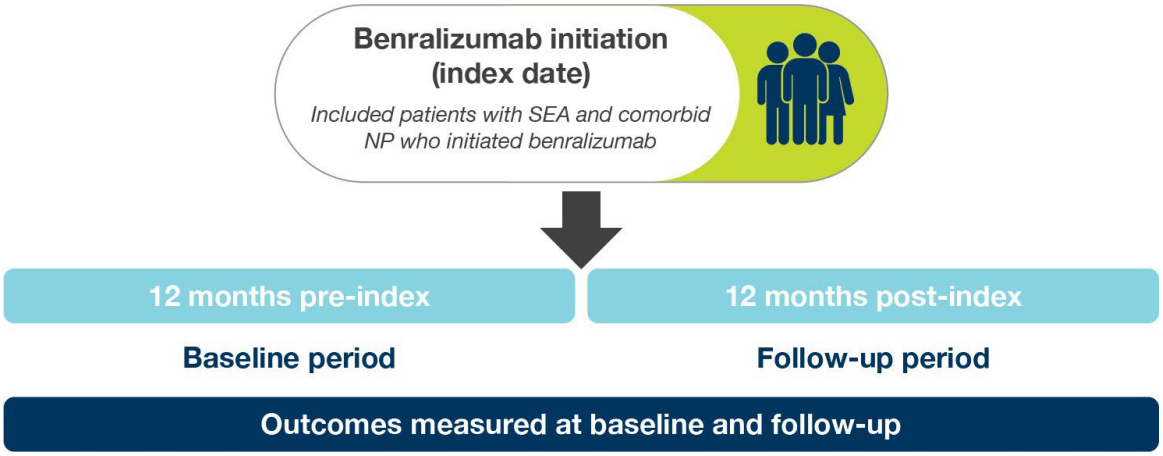
## Supplemental appendix

**Supplementary Figure 1.** Study design




NP, nasal polyps; SEA, severe eosinophilic asthma.

**Supplementary Table 1.** Collaborators (RANS Principal Investigators and Investigators)

| **Principal investigators** | |
|---|---|
| France | Gilles Devouassoux |
| | Arnaud Bourdin |
| Germany | Ludger Klimek |
| Italy | Girolamo Pelaia |
| | Stefania Gallo |
| | Jan Walter Schroeder |
| | Massimo Triggiani |
| | Salvatore Lombardo |
| | Bianca Beghe |
| | Raffaele Campisi |
| Japan | Sachio Takeno |
| | Akira Yamasaki |
| Spain | Maria Gil |
| | Rafael Hijano |
| | Eva Martinez-Moragon |
| | Juan Maza-Solano |
| | Ana Rosado Ingelmo |
| | Julio Delgado Romero |
| | Manuel Jorge Rial Prado |
| | Irina Bobolea |
| | Javier Domínguez-Ortega |
| USA | Michael E Wechsler |
| | Li-Xing Man |
| | Joseph Han |
| | Robert Lin |
| | Alfred Iloreta Jr. |
| **Investigators** | |
| Italy | Annamaria Bosi |
| | Simone Rizzato |
| | Davide Celsi |
| | Martina Liuzzi |
| | Andrea Toniato |
| Japan | Takashi Ishino |
| | Hiroshi Iwamoto |
| | Naoko Higaki |
| Spain | Leticia de las Vecillas Sánchez |
| | Magdalena Lluch |
| USA | Paul D. Allen |
| | Maura Campbell |
| | Isaac L. Schmale |

**Supplementary Table 2.** Approving IRB and ethics committees

| Country | Organization | IRB and ethics committees' name |
|---|---|---|
| France | Hôpital de la Croix Rousse | Notification to Health Data Hub was required (registration number: 2021-A02475-36) |
| | CHU Montpellier - Hôpital Arnaud de Villeneuve | |
| | Assistance Publique Hopitaux de Marseille - Hospital Nord | |
| Italy | AOU Renato Dulbecco | Comitato Etico Regione Calabria Sez. Area Centro |
| | ASST Sette Laghi | Comitato Etico dell'Insubria/ the Insubria Ethics Committee |
| | ASST Grande Ospedale Metropolitano Niguarda | COMITATO ETICO AREA 3 |
| | Azienda Ospedaliero Universitaria Careggi | COMITATO ETICO REGIONE TOSCANA – AREA VASTA SUD EST |
| | A.O.U. San Giovanni di Dio Ruggi d'Aragona | COMITATO ETICO CAMPANIA SUD |
| | A.O.U. Policlinico di Modena | COMITATO ETICO DELL'AREA VASTA EMILIA NORD |
| | AORN Ospedali dei Colli -A.O. MONALDI | Comitato Etico Università degli Studi della Campania "Luigi Vanvitelli" |
| | Hematology Sapienza University | the Comitato Etico dell'Università Sapienza |
| | POLICLINICO UNIVERSITARIO PRESIDIO DI MONSERRATO | Comitato Etico Azienda Ospedaliero Universitaria di Cagliari/the Independent Ethics Committee of the Azienda Ospedaliero di Cagliari |
| | A.O.U. Policlinico V. Emanuele - Presidio Gaspare Rodolico | Comitato etico Catania 1 |
| Japan | Niigata University Medical and Dental Hospital | Ethical Committee for Epidemiology of Hiroshima University |
| | Hiroshima University Hospital | |
| | Kansai Medical University Medical Center | |
| | Nagaoka Red Cross Hospital | |
| | Tottori University Hospital | |
| | Showa University Hospital | |

| | | |
|---|---|---|
| Spain | Hospital Universitario 12 de Octubre | COMITÉ DE ÉTICA DE LA INVESTIGACIÓN CON MEDICAMENTOS (CEIM) del HOSPITAL UNIVERSITARIO 12 DE OCTUBRE/ the Clinical Research Ethics Committee of 12 de Octumbre University Hospital |
| | Hospital del Mar | |
| | Hospital Universitario Dr Peset | |
| | Hospital Universitario Virgen Macarena | |
| | Hospital Arnau de Vilanova de Valencia | |
| | Hospital de Especialidades de Jerez de la Frontera | |
| | Hospital Clínico Universitario de Salamanca | |
| | Hospital Universitario Fundación de Alcorcón | |
| | Hospital Universitario Virgen Macarena | |
| | Complejo Hospitalario Universitario A Coruña | |
| | Hospital Clínic Barcelona | |
| | Hospital Universitario La Paz | |
| United States of America | National Jewish Medical & Research Center | WCG IRB (WCG has combined its five IRBs into a single IRB called “WCG IRB.” This includes Western IRB, Copernicus Group IRB, Aspire IRB, New England IRB, and Midlands IRB) |
| | University of Rochester Medical Center | |
| | Eastern Virginia Med. School, Norfolk | |
| | IMMUNOe Research Centers | |
| | New York Allergy And Sinus Centers - Glendale | |
| | Mount Sinai | |

**Supplementary Table 3.** Systemic corticosteroid use at baseline (12-month pre-index period) and follow-up period after benralizumab initiation

| Treatment | Baseline | Follow-up (up to 12 months) |
|---|---|---|
| **SCS use for asthma only** | | |
| SCS, n/N (%) | 95/233 (40.8) | 28/233 (12.0) |
| | n=91 | n=28 |
| Number of SCS courses[a], mean (SD) | 2.4 (2.4) | 2.5 (2.4) |
| Total daily dose (mg)[a], mean (SD) | n doses=215 | n doses=69 |
| | 29.7 (37.1) | 29.1 (26.1) |
| Total duration of use (days)[a,b], mean | n=94 | n=28 |
| (SD) | 251.6 (1209.7) | 92.9 (239.5) |
| **SCS use for NP only** | | |
| SCS, n/N (%) | 17/233 (7.3) | 11/233 (4.7) |
| Number of SCS courses[a], mean (SD) | n=17 | n=11 |
| | 1.5 (0.7) | 2.3 (2.57) |
| Total daily dose (mg)[a], mean (SD) | n doses=26 | n doses=25 |
| | 28.2 (10.3) | 27.1 (21.6) |
| Total duration of use (days)[a,b], mean | n=17 | n=11 |
| (SD) | 69.2 (178.4) | 96.5 (200.7) |

**Notes:** Prior treatments are those which are started and stopped on or before the index date.

[a]Among those prescribed that medication; SCS doses presented as prednisone equivalents. [b]Includes days the patient was on SCS, regardless of dose.

**Abbreviations:** SCS, systemic corticosteroid; SD, standard deviation.

**Supplementary Table 4.** Change from baseline (12-month pre-index period) in total NPS following benralizumab initiation by subgroup[a]

| | Total NPS, mean (SD) | | Mean change from baseline in total NPS[b] (95% CI) |
|---|---|---|---|
| | Baseline (12-month pre-index period) | Follow-up (up to 12 months) | |
| All patients | n=91 | n=63 | n=57 |
| | 3.8 (2.4) | 3.0 (2.1) | –1.2 (–1.7, –0.6) |
| Patients with baseline total NPS <5 | n=56 | n=33 | n=33 |
| | 2.3 (1.5) | 2.2 (1.7) | –0.4 (–0. 9, 0.0) |
| Patients with baseline total NPS ≥5 | n=35 | n=24 | n=24 |
| | 6.3 (0.9) | 4.1 (2.2) | –2.2 (–3.2, –1.2) |
| Patients with no baseline NP surgery[c] | n=75 | n=53 | n=47 |
| | 3.9 (2.3) | 3.3 (2.0) | –1.0 (–1.5, –0.5) |
| Patients with no NP surgery at any time pre-index | n=38 | n=26 | n=25 |
| | 4.5 (2.0) | 3.4 (1.9) | –1.3 (–2.2, –0.4) |
| Patients with NP surgery at any time pre-index | n=50 | n=35 | n=30 |
| | 3.3 (2.5) | 2.8 (2.2) | –1.0 (–1.8, –0.3) |
| Baseline blood eosinophil count ≥300 cells/µL | n=64 | n=49 | n=45 |
| | 3.9 (2.1) | 3.0 (1.9) | –1.1 (–1.7, –0.6) |

**Notes:** [a]Only subgroups with a minimum of 20 patients were assessed. [b]Changes from baseline were evaluated in the subset of patients who had both baseline and follow-up available data. [c]NP surgery within 12 months pre-index.

**Abbreviations:** CI, confidence interval; NP, nasal polyps; NPS, Nasal Polyp Score; SD, standard deviation.

**Supplementary Table 5.** Change from baseline (12-month pre-index period) in SNOT-22 total score following benralizumab initiation by subgroup[a]

| | SNOT-22 total score, mean (SD) | | Mean change from baseline in SNOT-22 total score (95% CI) |
|---|---|---|---|
| | Baseline (12-month pre-index period) | Follow-up (up to 12 months) | |
| All patients | n=161 | n=114 | n=105 |
| | 47.5 (22.6) | 28.9 (21.1) | –19.8 (–23.6, –15.9) |
| Patients with baseline SNOT-22 score[b] | | | |
| 8–20 (mild) | n=16 | n=11 | n=11 |
| | 14.6 (3.7) | 9.6 (9.1) | –5.1 (–11.3, 1.1) |
| >20–50 (moderate) | n=59 | n=38 | n=38 |
| | 37.4 (7.5) | 24.3 (15.7) | –13.2 (–18.2, –8.3) |
| ≤50 (mild/moderate) | n=75 | n=49 | n=49 |
| | 32.5 (11.6) | 21.0 (15.7) | –11.4 (–15.5, –7.3) |
| >50 (severe) | n=78 | n=53 | n=53 |
| | 66.4 (12.2) | 36.8 (21.3) | –28.6 (–34.4, –22.8) |
| Patients with no baseline NP surgery[c] | n=139 | n=104 | n=95 |
| | 48.4 (22.6) | 28.9 (21.2) | –20.4 (–24.4, –16.4) |
| Patients with no NP surgery at any time pre-index | n=69 | n=52 | n=48 |
| | 49.7 (19.9) | 28.0 (20.7) | –21.2 (–27.1, –15.2) |
| Patients with NP surgery at any time pre-index | n=86 | n=59 | n=54 |
| | 46.3 (24.3) | 28.9 (21.0) | –20.1 (–25.2, –14.9) |
| Baseline blood eosinophil count ≥300 cells/µL | n=118 | n=92 | n=86 |
| | 51.1 (21.8) | 28.8 (20.6) | –21.5 (–25.7, –17.2) |

**Notes:** [a]Only subgroups with a minimum of 20 patients were assessed. [b]Eight patients with baseline SNOT-22 score <8 were excluded from all subgroups.

[c]NP surgery within 12 months pre-index.

**Abbreviations:** CI, confidence interval; NP, nasal polyps; SNOT-22, SinoNasal Outcome Test-22; SD, standard deviation.

**Supplementary Table 6.** Change from baseline (12-month pre-index period) in NPS and SNOT-22 score following benralizumab initiation by countries[a]

| Country | Measures | Baseline | Follow-up (up-to 12 months) |
|---|---|---|---|
| France | **SNOT-22** | n=27 | n=23 |
| | Total score, mean (SD) | 49.9 (24.7) | 34.0 (22.6) |
| | Change from baseline[b], mean (95% CI) | N/A | –14.5 (–20.4, –8.6) |
| | Percent with clinically significant improvement, n/N (%) | N/A | 16/22 (72.7) |
| Italy | **SNOT-22** | n=89 | n=61 |
| | Total score, mean (SD) | 50.2 (21.3) | 27.7 (20.9) |
| | Change from baseline[a], mean (95% CI) | N/A | –24.4 (–30.3, –18.6) |
| | Percent with clinically significant improvement, n/N (%) | N/A | 41/57 (71.9) |
| Spain | **Total NPS** | n=33 | n=28 |
| | Total NPS, mean (SD) | 4.4 (2.0) | 3.3 (1.7) |
| | Change from baseline[a], mean (95% CI) | N/A | –1.1 (–1.8, –0.4) |
| | Percent with clinically significant improvement, n/N (%) | N/A | 13/23 (56.5) |

**Notes:** [a]Only subgroups with a minimum of 20 patients were assessed. [b]Changes from baseline were evaluated in the subset of patients who had both baseline and follow-up available data.

**Abbreviations:** CI, confidence interval; N/A, not applicable; NP, nasal polyps; NPS, Nasal Polyp Score; SNOT-22, SinoNasal Outcome Test-22; SD, standard deviation.