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Laboratory safety of dupilumab in moderate-to-severe atopic dermatitis: results from three phase III trials (LIBERTY AD SOLO 1, LIBERTY AD SOLO 2, LIBERTY AD CHRONOS)

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What's already known about this topic?

- Long-term treatment of atopic dermatitis (AD) with conventional immunosuppressive agents is limited by risk of significant side effects and a need for repeated tests to monitor haematological and/or organ (e.g. liver, kidney) toxicities.
- Dupilumab (monoclonal antibody blocking the shared receptor subunit for interleukin-4 and interleukin-13) is approved for treatment of patients with inadequately controlled, moderate-to-severe AD.
- In 16-week and 52-week studies, dupilumab demonstrated a positive benefit/risk profile in moderate-to-severe AD.

What does this study add?

- This study is the first comprehensive analysis of dupilumab laboratory safety data of the 16-week SOLO 1 and SOLO 2 (pooled $N = 1376$) and 52-week CHRONOS ($N = 740$) trials, demonstrating absence of clinically important changes in haematology, serum chemistry and urinalysis parameters in patients with moderate-to-severe AD treated with dupilumab.
- Our data support the use of dupilumab as a systemic treatment for long-term management of moderate-to-severe AD without routine laboratory monitoring in clinical practice.

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Summary

Background Dupilumab (monoclonal antibody blocking the shared receptor subunit for IL-4 and IL-13) is approved for patients aged ≥ 12 years with inadequately controlled, moderate-to-severe atopic dermatitis (AD). Dupilumab trials of up to 52 weeks demonstrated efficacy and a favourable safety profile in patients with moderate-to-severe AD inadequately controlled with topical medications.

Objective To further characterise the safety of dupilumab by evaluating clinical laboratory findings from three randomised, double-blinded, placebo-controlled phase III trials (LIBERTY AD SOLO 1 & 2 and LIBERTY AD CHRONOS).

Methods Patients were randomised 1:1:1 (SOLO 1 & 2) or 3:1:3 (CHRONOS) for 16 and 52 weeks, respectively, to dupilumab weekly, every 2 weeks or placebo. CHRONOS patients received a standardised concomitant topical corticosteroid regimen. Laboratory outcomes were summarised descriptively in 1376 patients from SOLO 1 & 2 and 740 from CHRONOS.

Results Treatment groups had similar results in baseline laboratory parameters. Platelets and neutrophils showed mild decreases from baseline in dupilumab vs. placebo groups. Some dupilumab-treated patients had small transient increases in eosinophils. Grade 3 eosinophilia was reported in $< 1\%$ of dupilumab-treated and placebo-treated patients; no adverse events were associated with eosinophilia. Lactate dehydrogenase levels decreased from baseline during dupilumab treatment in all trials. No clinically meaningful changes were observed between treatment groups in other haematology, chemistry or urinalysis parameters.

Conclusions There were no clinically important changes in routine laboratory parameters that could be attributed to dupilumab. This study supports use of dupilumab as a systemic treatment for moderate-to-severe AD that does not require laboratory monitoring.

Atopic dermatitis (AD) is a common, chronic and relapsing inflammatory skin disorder characterised by intense pruritus and eczematous lesions.¹ AD is associated with disruption of the skin barrier and immune-mediated abnormalities with skewing towards type 2 immune responses^{2,3} and increased susceptibility of patients to cutaneous infections, including *Staphylococcus aureus* colonisation, eczema herpeticum⁴ and non-cutaneous or systemic infections.^{5,6} Topical corticosteroids (TCS) and calcineurin inhibitors (TCI) remain the mainstay of AD therapy;^{7,8} however, moderate-to-severe AD often cannot be adequately controlled with topical treatments and requires use of systemic agents.⁹ Currently, oral corticosteroids (e.g. prednisolone) are approved by the US Food and Drug Administration (FDA) for treatment of inflammatory skin diseases, but they are only recommended in short courses for AD, and their use should be limited to specific circumstances such as a lack of other adequate treatment options or during episodes of acute flares where immediate relief is required.¹⁰ Among conventional immunosuppressants, only ciclosporin has approval, limited to short-term treatment of severe AD in most European countries and Japan. Other off-label systemic medications are also used in clinical practice, including azathioprine, mycophenolate mofetil and methotrexate.^{8,11–15} Long-term treatment of AD with systemic immunosuppressive agents is limited by safety concerns and a need for repeated tests to monitor clinical laboratory abnormalities and/or organ (e.g. liver and kidney) toxicities.^{8,11–15} Dupilumab, a fully human VelocImmune[®]-derived^{16,17} monoclonal antibody, blocks the shared receptor subunit for interleukin (IL)-4 and IL-13, thus inhibiting signalling of both IL-4 and IL-13. These cytokines are key drivers of type 2 inflammatory diseases such as AD as well as asthma, allergic rhinitis and food allergies, which are common AD comorbidities.¹⁸ Dupilumab is approved for subcutaneous (SC) administration at 300 mg every 2 weeks

(q2w) for the treatment of patients aged 12 years and older in the USA with moderate-to-severe AD inadequately controlled with topical prescription therapies or when those therapies are not advisable,¹⁹ for the treatment of adult AD patients not adequately controlled with existing therapies in Japan and for use in adults with moderate-to-severe AD who are candidates for systemic therapy in the EU.²⁰ Dupilumab is also approved by the US FDA as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma; and as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyps.¹⁹ Three phase III clinical trials of dupilumab (LIBERTY AD SOLO 1 [NCT02277743], LIBERTY AD SOLO 2 [NCT02277769], LIBERTY AD CHRONOS [NCT02260986]) have demonstrated efficacy in improving AD signs, symptoms and quality of life and showed a favourable safety profile for treatment durations of 16 weeks (SOLO 1 & 2) and 52 weeks (CHRONOS) in patients with moderate-to-severe AD with inadequate response to topical medications.^{21–23} Other randomised, placebo-controlled trials in patients with AD, as well as randomised, placebo-controlled trials in other diseases mediated by type 2 inflammation, including asthma, chronic sinusitis with nasal polyps and eosinophilic oesophagitis, demonstrated similar results.^{24–33} Due to its selective targeting of type 2 inflammation, dupilumab has not been associated with significant infection-related adverse events (AEs) often seen with monoclonal antibodies that affect type 1-mediated immune responses, such as anti-tumour necrosis factor alpha (anti-TNF α) therapies.^{21,22,26,34,35} However, in most dupilumab AD trials, higher incidences of conjunctivitis were observed in dupilumab vs. placebo groups; most cases were mild-to-moderate, and most recovered/resolved during the treatment period.³⁶ Conjunctivitis incidence was very low and similar for dupilumab and placebo in other type 2 diseases.³⁶

To further characterise the safety profile of dupilumab, we evaluated clinical laboratory data from three large, randomised, double-blinded, placebo-controlled phase III trials in adult patients with moderate-to-severe AD.

Patients and methods

Study design

SOLO 1, SOLO 2 and CHRONOS were randomised, double-blinded, placebo-controlled phase III trials, conducted in adherence with the Declaration of Helsinki principles. All patients provided signed written informed consent prior to performing any study procedures. Institutional review boards and independent ethics committees reviewed and approved the protocols, informed consent forms and patient information prior to study initiation.

Study designs and patient populations have been described previously.^{21,22} Briefly, SOLO 1 & 2 had identical study designs. Patients were randomised 1:1:1 to monotherapy with SC dupilumab 300 mg weekly (qw), dupilumab 300 mg q2w or placebo qw for 16 weeks. Key inclusion criteria were: AD inadequately controlled with or inadvisable for topical medications; age ≥ 18 years; moderate-to-severe AD for ≥ 3 years prior to screening; Investigator's Global Assessment (IGA) score ≥ 3 (moderate-to-severe; scale 0–4) and Eczema Area and Severity Index (EASI) ≥ 16 (scale 0–72).²¹ In CHRONOS, patients were randomised 3:1:3 to receive SC dupilumab 300 mg qw, dupilumab 300 mg q2w or placebo qw for 52 weeks. All patients received concomitant medium-potency TCS, or low-potency TCS in thin or sensitive skin areas (e.g. face or neck); TCI could be used in certain areas such as the face and intertriginous areas, if not used concomitantly with TCS to treat the same areas. Once lesions were clear/almost clear, TCS $\pm$ TCI could be tapered, then stopped. Key inclusion criteria were: documented history of inadequate response to medium-to-high-potency TCS and/or documented systemic treatment use within the last 6 months; AD inadequately controlled with or inadvisable for topical medications; age ≥ 18 years; moderate-to-severe AD for ≥ 3 years prior to screening; IGA ≥ 3 (moderate-to-severe; scale 0–4) and EASI ≥ 16 (scale 0–72).²²

Safety analysis

The safety analysis set (SAF) included all randomised patients who received any study drug; it was based on the treatment received (as treated); for CHRONOS, this includes patients who had completed treatment as of the cut-off date for FDA submission of the dupilumab biologics license application,²² as well as those whose treatment was still ongoing after the FDA submission. If a patient received a dose regimen different to that assigned during the study, this patient was considered as treated by the lowest active dose. SOLO 1 & 2 data were pooled. Safety assessments included clinical laboratory evaluations (haematology, clinical chemistry and urinalysis) and reported AEs. For patients who discontinued study treatment, laboratory data were collected during subsequent monitoring visits, but no laboratory data were collected after withdrawal from the study. Blood samples for testing of haematology and chemistry parameters were collected at baseline and pre-specified post-baseline time points, including at the end of the treatment period. Blood samples were collected after a 6- to 8-hour fast, if possible; fasting was not mandatory. Haematology, serum chemistry and urinalysis samples were analysed by a central laboratory (SOLO 1 & 2: PPD Laboratories, Highland Heights, KY, USA; CHRONOS: Covance Laboratories, Indianapolis, IN, USA). All untoward medical occurrences, including medically relevant laboratory abnormalities, were considered AEs according to the protocol definition. The number and proportion of patients reporting treatment-emergent adverse events (TEAEs) were listed by Medical Dictionary for Regulatory Activities (MedDRA) system Preferred Terms (PTs). All safety outcomes were assessed using descriptive statistics.

Laboratory variables

Haematology analyses covered haematocrit, haemoglobin, red blood cells, white blood cells, red cell indices and platelet count. Further differential outcomes included neutrophils, lymphocytes, monocytes, basophils and eosinophils.

Serum chemistry analyses covered metabolic function parameters including albumin, creatine phosphokinase (CPK; CPK isoenzymes were measured when CPK was > 5 times the upper limit of normal [ULN]), glucose, haemoglobin A1C and total serum protein; electrolyte parameters including bicarbonate, calcium, chloride, potassium and sodium; renal function parameters including blood urea nitrogen, creatinine and uric acid; liver function parameters including alkaline phosphatase, alanine transaminase, aspartate transaminase, total bilirubin (direct and indirect bilirubin were measured when the total bilirubin was above the ULN) and lactate dehydrogenase (LDH) as well as lipid profile parameters including total cholesterol, low-density lipoprotein, high-density lipoprotein and triglycerides. Urinalysis included testing of pH and specific gravity.

Statistical methods

All laboratory data analyses were descriptive; there were no statistical comparisons of treatment groups for any laboratory variables. All data were summarised as observed, and no imputations were used for missing data.

Results

Baseline

Clinical laboratory data were assessed in 1376 patients from SOLO 1 & 2 (SAF for pooled data: placebo, $n = 456$; dupilumab q2w, $n = 465$; dupilumab qw, $n = 455$) and 740 patients from CHRONOS (SAF: placebo + TCS, $n = 315$; dupilumab q2w + TCS, $n = 110$; dupilumab qw + TCS, $n = 315$). Baseline haematology, serum chemistry and urinalysis characteristics were balanced across treatment groups (Tables S1a, b; Tables S2a–e; Table S3; see Supporting Information). Baseline serum levels of LDH, a marker of tissue damage that correlates with AD disease activity and severity, were elevated in a large proportion of patients (Table S2d; see Supporting Information); details are provided below. In SOLO 1 & 2, 372 (81.6%; placebo), 435 (93.5%; dupilumab q2w) and 413 (90.8%; dupilumab qw)

patients completed the 16-week study treatment period; in CHRONOS, 225 (71.4%; placebo + TCS), 95 (86.4%; dupilumab q2w + TCS) and 276 (87.3%; dupilumab qw + TCS) patients completed the 52-week study treatment period.

Clinical laboratory parameters during the treatment period

Platelets

Platelet values for the dupilumab and placebo groups were within normal ranges, with greater decreases from baseline in the dupilumab groups than the placebo groups (Fig. 1a, b; Table S1a; see Supporting Information). In SOLO 1 & 2, the mean change from baseline to week 16 for platelets ($\times 10^9/L$) was -3.1 , -5.7 and -11.2 for placebo, dupilumab q2w and dupilumab qw, respectively; for baseline to week 52 in CHRONOS, these values were -2.2 , -12.9 and -13.1 , for placebo + TCS, dupilumab q2w + TCS and dupilumab qw + TCS, respectively. These changes in platelet counts were of no particular clinical concern and did not necessitate additional testing or changes to treatment. Moreover, no notable differences in platelet counts were observed between treatment groups in shifts from normal values at baseline to high or low values during the study period (Table S4a; see Supporting Information). For patients with grade 2 (platelet count: $100 \times 10^9/L$ to $124 \times 10^9/L$ [moderate])³⁷ and grade 3 ($25 \times 10^9/L$ to $99 \times 10^9/L$ [severe])³⁷ thrombocytopenia, magnitudes of change in platelet counts from baseline were similar across the dupilumab and placebo groups (Fig. 2a). One patient in the placebo group in SOLO 1 had grade 4 thrombocytopenia (platelet count $< 25 \times 10^9/L$ [potentially life-threatening])³⁷ at week 8 (Table 1a). Grade 3 thrombocytopenia incidence rates were $< 1\%$ across all treatment groups (Fig. 1c; Table 1a).

Neutrophils

Neutrophil values were within normal ranges across all treatment groups, with greater decreases from baseline in the dupilumab groups vs. placebo groups in SOLO 1 & 2 (mean change from baseline to week 16 [$\times 10^9/L$]: -0.1 , -0.4 and -0.5 for placebo, dupilumab q2w

and dupilumab qw, respectively) and CHRONOS (mean change from baseline to week 52 [$\times 10^9/L$]: -0.2 , -0.6 and -0.6 for placebo + TCS, dupilumab q2w + TCS and dupilumab qw + TCS, respectively) (Fig. 3a, b; Table S1b; see Supporting Information). These changes in neutrophil counts were of no particular clinical concern and did not necessitate additional testing or changes to treatment. Moreover, no notable differences in neutrophil counts were observed between treatment groups in shifts from normal values at baseline to high or low values during the study period (Table S4b; see Supporting Information). Patients with grade 2 (neutrophil count: $1.0 \times 10^9/L$ to $1.499 \times 10^9/L$ [moderate])³⁷ and grade 3 ($0.5 \times 10^9/L$ to $0.999 \times 10^9/L$ [severe])³⁷ neutropenia had lower neutrophil counts at baseline than the overall study populations (Fig. 2b; Table S1b; see Supporting Information, and the magnitudes of change in neutrophil counts from baseline in this subset of patients were similar across dupilumab and placebo groups (Fig. 2b). No patient had neutropenia grade 4 (neutrophil count $< 0.5 \times 10^9/L$ [potentially life-threatening]). Grade 3 neutropenia incidence rates were $< 1\%$ across all treatment groups (Fig. 3c; Table 1b).

Eosinophils

In SOLO 1 & 2, the dupilumab groups had greater mean and median initial increases from baseline in eosinophil counts than the placebo groups, with the highest increase observed at week 4 (Fig. 4a, b; Table S1b; see Supporting Information). Eosinophils returned to near-baseline levels by week 16 (mean change [$\times 10^9/L$], baseline to week 16: -0.2 , -0.0 and -0.0 , for placebo, dupilumab q2w and dupilumab qw, respectively). By contrast, there was no such eosinophil increase in the overall study population in CHRONOS (mean change [$\times 10^9/L$] baseline to week 52: -0.2 , -0.2 and -0.2 , for placebo + TCS, dupilumab q2w + TCS and dupilumab qw + TCS, respectively) (Fig. 4a, b; Table S1b; see Supporting Information). A higher proportion of patients in the dupilumab groups vs. placebo had shifts from normal eosinophil counts at baseline to high ($> ULN$) values throughout the treatment period in SOLO 1 & 2 (for dupilumab q2w and qw, respectively vs. placebo; week 4, 12.6% and 13.2% vs. 9.0%; week 16, 9.5% and 14.8% vs. 6.2%) and CHRONOS (for dupilumab q2w +

TCS and qw + TCS, respectively vs. placebo + TCS; week 4, 9.1% and 9.6% vs. 7.8%, week 52, 14.5% and 9.1% vs. 6.7%) (Table S4c; see Supporting Information). In the subset of patients with grade 2 (eosinophil count: $1.501 \times 10^9/L$ to $5.0 \times 10^9/L$ [moderate])³⁷ and grade 3 (eosinophil count: $> 5.0 \times 10^9/L$ [severe])³⁷ eosinophilia, small initial increases in absolute mean counts were observed in all treatment groups in SOLO 1 & 2 and CHRONOS, with a trend to return to near baseline levels; this was particularly evident in CHRONOS (Fig. 2c). Incidence rates of treatment-emergent eosinophilia were numerically higher in the dupilumab groups in all three trials (Fig. 4c; Table 1c). Grade 3 treatment-emergent eosinophilia was reported in < 1% of dupilumab-treated and placebo-treated patients (Fig. 4c; Table 1c). The transient increases in eosinophils had no apparent clinical consequences, as dupilumab-treated patients with high eosinophil counts did not show any clinical manifestations or high frequency of AEs (Table S5; see Supporting Information).

LDH

LDH levels were elevated at baseline (median, 231.0–247.0; Table S2d; see Supporting Information). At baseline, 25.2–27.0% of patients in SOLO 1 & 2 and 50.5–57.3% of patients in CHRONOS had levels above the ULN (per central laboratory determination; normal ranges: SOLO 1 & 2, males: 135.0–281.0 IU/L, females: 135.0–330.0 IU/L; CHRONOS, 53.0–234.0 IU/L [both sexes]). Serum LDH decreased over time in SOLO 1 & 2 (mean change from baseline to week 16: -26.2, -69.7 and -76.0 IU/L for placebo, dupilumab q2w and dupilumab qw, respectively) and CHRONOS (mean change, baseline to week 52: -49.7, -88.2 and -85.1 IU/L for placebo + TCS, dupilumab q2w + TCS and dupilumab qw + TCS, respectively) (Fig. 5a, b; Table S2d; see Supporting Information). A higher proportion of patients in the dupilumab groups vs. placebo had shifts from high LDH at baseline to normal values throughout the treatment period (Fig. 5c; Table S4d; see Supporting Information).

Other laboratory parameters

No changes in other haematology (Table S1a, b; see Supporting Information), serum chemistry and urinalysis (Table S2a–e; Table S3; see Supporting Information) parameters in any of the treatment groups were of clinical concern or necessitated additional testing or changes to treatment.

Treatment withdrawal

Three patients discontinued study treatment due to abnormal laboratory values (Fig. S1a–c; see Supporting Information). These included one patient in the dupilumab qw group in SOLO 1 with a TEAE of lymphocytosis, which was not considered by the investigator to be related to dupilumab; and one patient each in the dupilumab q2w group in SOLO 2 and the placebo + TCS group in CHRONOS with TEAEs of neutropenia, which were considered by the investigators to be related to study drug. The patients in SOLO 1 & 2 continued to be monitored to week 16, whereas the CHRONOS patient withdrew from the study and was not monitored after week 8. No other laboratory test abnormalities led to treatment discontinuation in these studies. There were no notable differences in the laboratory results for the patients who withdrew due to haematological changes or patients who discontinued due to any TEAEs compared with the general patient population, other than those that would be expected for those particular patients (Tables S6a–b; see Supporting Information).

Adverse events

AEs reported for the overall study populations in SOLO 1 & 2 and CHRONOS were previously published.^{21,22} Overall, similar rates of TEAEs were reported across treatment groups during these studies. The overall incidence of infections was similar in patients treated with dupilumab and placebo.^{21,22,34} Conjunctivitis (both MedDRA PT “conjunctivitis” and a compiled term for any PT with the word “conjunctivitis”) and injection-site reactions (MedDRA high-level term) were more frequent in patients treated with dupilumab.^{21,22,36} Higher rates of AD exacerbations (MedDRA PT) and non-herpetic skin infections

(adjudicated) were reported in the placebo groups. Laboratory outcomes that were serious adverse events (SAEs) were rare: one patient (0·5%) in SOLO 1 had an SAE of anaemia; one (0·4%) in SOLO 2 had an SAE of thrombocytopenia and one (0·3%) in CHRONOS had an SAE of liver function test abnormal (MedDRA PTs); all were in the placebo group in their respective studies.²²⁻²⁴

Discussion

This analysis of more than 2000 patients from three large phase III placebo-controlled studies did not reveal any adverse changes in laboratory parameters that could be attributed to dupilumab. None of the reported changes necessitated additional testing or changes to treatment. Mean and median haematology and serum chemistry laboratory values were generally consistent with baseline values or showed small changes from baseline. Small decreases from baseline were noted for platelets and neutrophils within the dupilumab vs. placebo groups, which may reflect a decrease in systemic inflammation and AD severity.³⁸⁻⁴² Overall, platelet and neutrophil counts remained within the normal range at any visit, and the changes were not clinically meaningful for any treatment group.

Transient and usually mild-to-moderate increases in eosinophils were observed in a small number of patients treated with dupilumab in these studies; no AEs were attributed to eosinophilia. Of note, eosinophilia was less marked in patients treated with dupilumab + TCS in CHRONOS, suggesting that concomitant use of TCS may blunt the effect on eosinophils seen in the monotherapy studies.⁴³ Blood and tissue eosinophilia are characteristic of AD and other atopic diseases and correlate with disease activity.⁴⁴⁻⁴⁹ Type 2 inflammation mediated by IL-4, IL-13 and IL-5 promotes eosinophil growth, differentiation and trafficking to sites of inflammation.⁵⁰ Moreover, IL-4 and IL-13 regulate the expression of eotaxin-1 (C-C motif chemokine 11 [CCL11]), eotaxin-3 (CCL26), RANTES (CCL5) and MCP-4 (CCL13), potent chemoattractants for eosinophils.⁵¹⁻⁵⁴ IL-4 and IL-13 also induce vascular cell adhesion molecule 1 (VCAM-1) on endothelial cells, which is an adhesion molecule involved in

eosinophil transmigration.^{51–54} IL-4 and IL-13 promote eosinophil recruitment to sites of inflammation by increasing production of these chemokines and VCAM-1.^{47,50–52,54} In lesional skin of AD patients, dupilumab decreased eotaxin-3 and MCP-4.^{27,55} In mouse models of asthma, dupilumab blockage of IL-4 and IL-13 signalling prevents eosinophils from entering tissue, and hence eosinophils accumulate in the bloodstream.^{56,57} Hence, the transient increases in circulating eosinophils observed in a subset of patients could be a result of dupilumab inhibiting IL-4/IL-13–induced migration of eosinophils from the bloodstream into tissues.^{50,58} The fact that this phenomenon is not observed in every dupilumab-treated AD patient suggests that net effects on eosinophil counts are dependent on the magnitude of chemokine suppression and the rate of eosinophil production in a given patient. Of note, higher baseline levels of circulating eosinophils have been associated with increased incidence of conjunctivitis in both placebo-treated and dupilumab-treated patients in clinical trials in AD.³⁶ In monotherapy studies, patients with high baseline eosinophil levels reported 0·03–0·15 events of conjunctivitis per 100 patient-years (PY) for placebo and dupilumab combined, respectively, while patients with low baseline levels reported 0·02–0·03 events per 100 PY.³⁶ Similarly, in CHRONOS, patients with high eosinophils at baseline had 0·04–0·13 conjunctivitis events per 100 PY, respectively for placebo + TCS and dupilumab qw + TCS vs. 0·03–0·05 events per 100 PY for patients with low baseline eosinophil levels;³⁶ similar associations were also observed for baseline levels of the biomarkers thymus and activation-regulated chemokine (TARC) and IgE.³⁶ AD severity is associated with biomarker levels as well as with incidence of conjunctivitis, suggesting that the association of these biomarkers with conjunctivitis may result from their relationship to AD severity.³⁶

A decrease in LDH levels from baseline was seen during dupilumab treatment regardless of dose regimen in all trials. More dupilumab-treated patients achieved normalisation of LDH during the treatment period compared with placebo-treated patients. LDH is an intracellular enzyme that is widely expressed in tissues such as the skin.^{59–61} It is a biomarker of tissue

damage, and serum LDH concentrations have been reported to correlate with AD disease activity and severity.^{60–63}

No clinically meaningful changes were observed between treatment groups for other haematology, chemistry or urinalysis parameters. Overall, dupilumab was well tolerated in patients with moderate-to-severe AD with and without concomitant TCS use; both dupilumab dose regimens had acceptable safety profiles, which were generally comparable with that of placebo, apart from conjunctivitis and injection-site reactions.^{21–23} SAEs of laboratory outcomes were rare and were only reported in placebo-treated patients.

This analysis had limitations. These analyses included a total of 2116 patients; most (1376 in SOLO 1 & 2) received dupilumab for up to 16 weeks, and the remainder (740 in CHRONOS) for up to 52 weeks. These data showed that mean changes in laboratory parameters were transient and returned to near baseline levels during study treatment and were not associated with any clinical AEs, supporting the current guidance in the prescribing information that there is no requirement for routine laboratory monitoring; however, greater numbers of patients exposed to dupilumab for longer periods of time and in real-world situations will provide the sample sizes and more varied patient populations needed to discern rare events. Eligibility criteria for these trials excluded patients with serious concomitant health conditions; thus, further data are needed to determine laboratory monitoring needs for patients with the variety of conditions that may be encountered in a real-world setting.

In conclusion, although transient reductions in neutrophils and platelets as well as transient increases in blood eosinophils were observed in a small number of dupilumab-treated patients, they were not associated with any clinically significant AEs. The laboratory data described here, along with the efficacy and safety data provided in the previous reports of these studies, demonstrate that dupilumab results in a favourable benefit/risk ratio profile, further supporting the use of dupilumab as a systemic treatment for long-term management

of moderate-to-severe AD.^{21–23} Consistent with clinical trial data, EU²⁰ and US¹⁹ prescribing information do not require routine laboratory monitoring in clinical practice before initiation or during treatment with dupilumab. Because patient exclusion criteria in the dupilumab trials may have limited the variability of the study population, real-world evidence, including long-term data beyond 52 weeks of treatment, will provide additional valuable information on the role of laboratory monitoring in dupilumab-treated patients with AD.

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Table 1a. Proportion of patients with thrombocytopenia grades 1–4^a

Study week	Thrombo-cytopenia grade	SOLO 1 & 2, <i>n</i> (%)			CHRONOS, <i>n</i> (%)		
		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
0	1	1 (0.2)	1 (0.2)	0	0	3 (2.7)	1 (0.3)
	2	3 (0.7)	4 (0.9)	4 (0.9)	1 (0.3)	0	0
	3	1 (0.2)	2 (0.4)	1 (0.2)	0	0	1 (0.3)
	4	0	0	0	0	0	0
4	1	2 (0.4)	1 (0.2)	4 (0.9)	1 (0.3)	0	2 (0.6)
	2	1 (0.2)	3 (0.6)	2 (0.4)	0	0	0
	3	1 (0.2)	3 (0.6)	1 (0.2)	0	0	0
	4	0	0	0	0	0	0
8	1	4 (0.9)	1 (0.2)	1 (0.2)	0	1 (0.9)	3 (1.0)
	2	1 (0.2)	2 (0.4)	1 (0.2)	0	1 (0.9)	0
	3	0	3 (0.6)	0	0	0	0
	4	1 (0.2)	0	0	0	0	0
12	1	3 (0.7)	3 (0.6)	0	3 (1.0)	0	5 (1.6)
	2	1 (0.2)	5 (1.1)	2 (0.4)	1 (0.3)	0	0
	3	0	1 (0.2)	1 (0.2)	1 (0.3)	0	0
	4	0	0	0	0	0	0
16	1	1 (0.2)	3 (0.6)	2 (0.4)	0	0	1 (0.3)
	2	3 (0.7)	1 (0.2)	3 (0.7)	0	1 (0.9)	0
	3	0	2 (0.4)	0	1 (0.3)	0	1 (0.3)
	4	0	0	0	0	0	0
20	1				1 (0.3)	0	1 (0.3)
	2				1 (0.3)	1 (0.9)	0
	3				0	0	0
	4				0	0	0
28	1	n/a			1 (0.3)	0	3 (1.0)
	2				0	1 (0.9)	1 (0.3)
	3				0	0	0
	4				0	0	0
36	1				0	0	1 (0.3)

44	2	0	1 (0.9)	0
	3	0	0	0
	4	0	0	0
	1	0	0	0
	2	0	0	2 (0.6)
52	3	0	0	0
	4	0	0	0
	1	2 (0.6)	0	1 (0.3)
	2	0	1 (0.9)	1 (0.3)
	3	0	0	0
	4	0	0	0

^aThrombocytopenia grade scale follows the guidance provided by the US FDA:³⁷ platelet counts of $125 \times 10^9/\text{L}$ to $140 \times 10^9/\text{L}$ are defined as grade 1, $100 \times 10^9/\text{L}$ to $124 \times 10^9/\text{L}$ as grade 2, $25 \times 10^9/\text{L}$ to $99 \times 10^9/\text{L}$ as grade 3 and $< 25 \times 10^9/\text{L}$ as grade 4.

FDA, Food and Drug Administration; n/a, not applicable; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Table 1b. Proportion of patients with neutropenia grades 1–3^{a,b}

Study week	Neutropenia grade	SOLO 1 & 2, <i>n</i> (%)			CHRONOS, <i>n</i> (%)		
		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
0	1	11 (2.4)	8 (1.7)	14 (3.1)	3 (1.0)	1 (0.9)	5 (1.6)
	2	4 (0.9)	2 (0.4)	0	2 (0.6)	0	1 (0.3)
	3	0	0	0	0	0	0
4	1	7 (1.5)	22 (4.7)	28 (6.2)	5 (1.6)	5 (4.5)	10 (3.2)
	2	2 (0.4)	4 (0.9)	2 (0.4)	1 (0.3)	1 (0.9)	4 (1.3)
	3	0	0	0	0	0	0
8	1	12 (2.6)	22 (4.7)	23 (5.1)	4 (1.3)	3 (2.7)	11 (3.5)
	2	4 (0.9)	1 (0.2)	2 (0.4)	1 (0.3)	0	1 (0.3)
	3	0	0	1 (0.2)	0	0	0
12	1	11 (2.4)	22 (4.7)	24 (5.3)	2 (0.6)	1 (0.9)	11 (3.5)
	2	0	4 (0.9)	1 (0.2)	1 (0.3)	1 (0.9)	1 (0.3)
	3	1 (0.2)	0	0	0	0	1 (0.3)
16	1	9 (2.0)	16 (3.4)	15 (3.3)	4 (1.3)	1 (0.9)	6 (1.9)
	2	2 (0.4)	3 (0.6)	5 (1.1)	0	0	1 (0.3)
	3	0	1 (0.2)	0	0	0	0
20	1				9 (2.9)	2 (1.8)	3 (1.0)
	2				1 (0.3)	0	1 (0.3)
	3				0	0	0
28	1				4 (1.3)	3 (2.7)	11 (3.5)
	2				0	0	4 (1.3)
	3				0	0	0
36	1	n/a			5 (1.6)	8 (7.3)	8 (2.5)
	2				0	0	3 (1.0)
	3				0	0	0
44	1				8 (2.5)	3 (2.7)	8 (2.5)
	2				0	2 (1.8)	3 (1.0)
	3				0	0	0
52	1				2 (0.6)	4 (3.6)	8 (2.5)
	2				1 (0.3)	0	1 (0.3)

3

0

0

1 (0.3)

^aNeutropenia grade scale follows the guidance provided by the US FDA:³⁷ neutrophil counts of $1.5 \times 10^9/L$ to $2.0 \times 10^9/L$ are defined as grade 1, $1.0 \times 10^9/L$ to $1.499 \times 10^9/L$ as grade 2, $0.5 \times 10^9/L$ to $0.999 \times 10^9/L$ as grade 3 and $< 0.5 \times 10^9/L$ as grade 4. ^bNo patients in SOLO 1 & 2 and CHRONOS reported grade 4 neutropenia.

FDA, Food and Drug Administration; n/a, not applicable; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Table 1c. Proportion of patients with eosinophilia grades 1–3^a

Study week	Eosinophilia grade	SOLO 1 & 2, <i>n</i> (%)			CHRONOS, <i>n</i> (%)		
		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
0	1	109 (23.9)	111 (23.9)	131 (28.8)	90 (28.6)	29 (26.4)	57 (18.1)
	2	29 (6.4)	28 (6.0)	25 (5.5)	12 (3.8)	2 (1.8)	13 (4.1)
	3	1 (0.2)	0	0	0	1 (0.9)	1 (0.3)
4	1	104 (22.8)	113 (24.3)	102 (22.4)	51 (16.2)	16 (14.5)	42 (13.3)
	2	29 (6.4)	39 (8.4)	48 (10.5)	6 (1.9)	2 (1.8)	13 (4.1)
	3	0	3 (0.6)	2 (0.4)	0	1 (0.9)	0
8	1	79 (17.3)	92 (19.8)	105 (23.1)	47 (14.9)	21 (19.1)	45 (14.3)
	2	19 (4.2)	45 (9.7)	39 (8.6)	1 (0.3)	3 (2.7)	14 (4.4)
	3	0	1 (0.2)	3 (0.7)	0	1 (0.9)	0
12	1	84 (18.4)	86 (18.5)	95 (20.9)	34 (10.8)	19 (17.3)	53 (16.8)
	2	14 (3.1)	43 (9.2)	40 (8.8)	3 (1.0)	4 (3.6)	7 (2.2)
	3	0	0	1 (0.2)	0	0	0
16	1	81 (17.8)	99 (21.3)	91 (20.0)	44 (14.0)	22 (20.0)	49 (15.6)
	2	11 (2.4)	33 (7.1)	35 (7.7)	3 (1.0)	4 (3.6)	7 (2.2)
	3	0	2 (0.4)	1 (0.2)	0	0	0
20	1				27 (8.6)	20 (18.2)	37 (11.7)
	2				3 (1.0)	3 (2.7)	5 (1.6)
	3				0	1 (0.9)	1 (0.3)
28	1				32 (10.2)	14 (12.7)	37 (11.7)
	2				3 (1.0)	4 (3.6)	8 (2.5)
	3				0	0	1 (0.3)
36	1	n/a			29 (9.2)	18 (16.4)	42 (13.3)
	2				2 (0.6)	3 (2.7)	2 (0.6)
	3				0	0	0
44	1				29 (9.2)	17 (15.5)	33 (10.5)
	2				1 (0.3)	1 (0.9)	5 (1.6)
	3				0	0	0
52	1				28 (8.9)	15 (13.6)	29 (9.2)
	2				1 (0.3)	3 (2.7)	5 (1.6)

3

0

0

0

^aEosinophilia grade scale follows the guidance provided by the US FDA:³⁷ eosinophil counts of $0.65 \times 10^9/L$ to $1.5 \times 10^9/L$ are defined as grade 1, $1.501 \times 10^9/L$ to $5.0 \times 10^9/L$ as grade 2 and $> 5.0 \times 10^9/L$ as grade 3.

FDA, Food and Drug Administration; n/a, not applicable; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Figure legends

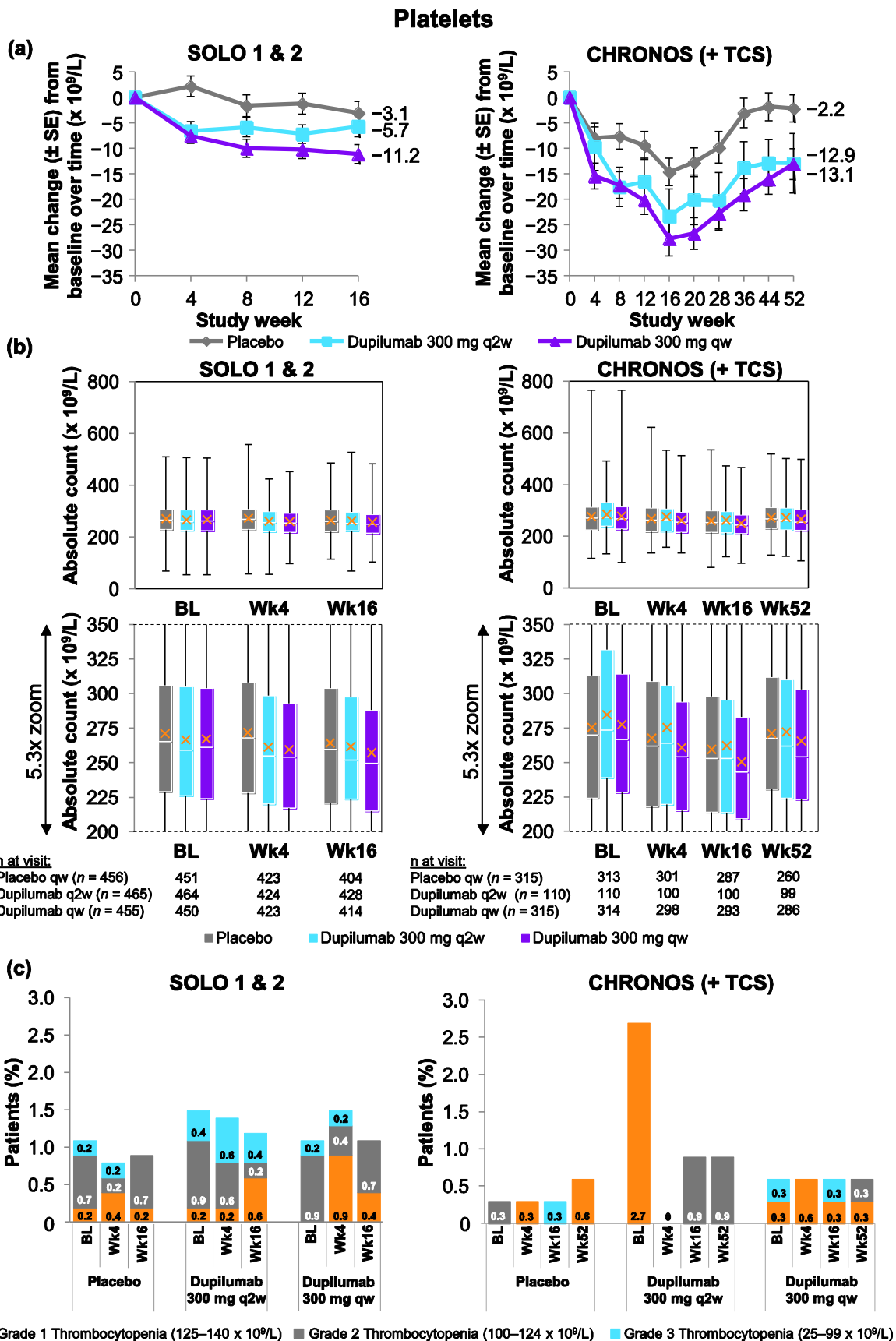
Fig 1. (a) Mean change in platelet count from baseline to week 16 (SOLO 1 & 2) and week 52 (CHRONOS). (b) Absolute platelet count. A close-up view of the box-and-whisker plots is depicted below. White horizontal lines indicate medians. X depicts mean values. Top and bottom of each box represent Q3 and Q2, respectively. Upper and lower vertical bars represent Q4 and Q1, respectively; horizontal segments on each end of the vertical bars represent minimum and maximum values. (c) Proportion of patients with thrombocytopenia grades 1–3; patient numbers are provided in Table 1a. Thrombocytopenia grade scale follows the guidance provided by the US FDA.³⁷ BL, baseline; FDA, Food and Drug Administration; *n*, number of patients; Q, quartile; qw, once weekly; q2w, every 2 weeks; SE, standard error; TCS, topical corticosteroids; Wk, week.

Fig 2. (a) Absolute mean platelet counts from baseline in the subset of patients with thrombocytopenia grades 2 and 3 through week 16 (SOLO 1 & 2) and week 52 (CHRONOS). (b) Absolute mean neutrophil counts from baseline in the subset of patients with neutropenia grades 2 and 3 through week 16 (SOLO 1 & 2) and week 52 (CHRONOS). (c) Absolute mean eosinophil counts from baseline in the subset of patients with eosinophilia grades 2 and 3 through week 16 (SOLO 1 & 2) and week 52 (CHRONOS). Toxicity grade scales follow the guidance provided by the US FDA.³⁷ FDA, Food and Drug Administration; qw, once weekly; q2w, every 2 weeks; SE, standard error; TCS, topical corticosteroids.

Fig 3. (a) Mean change in neutrophil count from baseline to week 16 (SOLO 1 & 2) and week 52 (CHRONOS). (b) Absolute neutrophil count. A close-up view of the box-and-whisker plots is depicted below. White horizontal lines indicate medians. X depicts mean values. Top and bottom of each box represent Q3 and Q2, respectively. Upper and lower vertical bars represent Q4 and Q1, respectively; horizontal segments on each end of the vertical bars represent minimum and maximum values. (c) Proportion of patients with neutropenia grades 1–3; patient numbers are provided in Table 1b. Neutropenia grade scale follows the guidance provided by the US FDA.³⁷ BL, baseline; *n*, number of patients; Q, quartile; qw, once weekly; q2w, every 2 weeks; SE, standard error; TCS, topical corticosteroids; Wk, week.

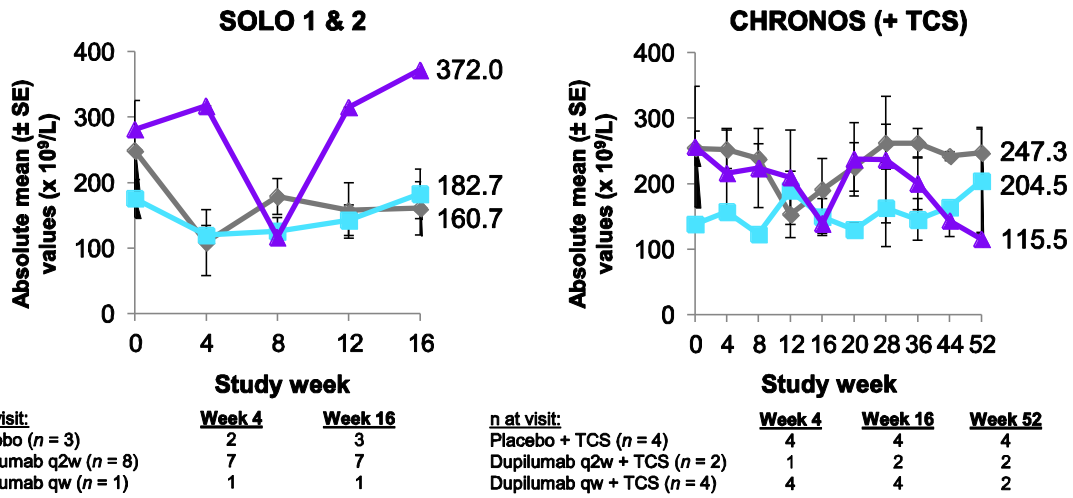
Fig 4. (a) Mean change in eosinophil count from baseline to week 16 (SOLO 1 & 2) and week 52 (CHRONOS). (b) Absolute eosinophil count. A close-up view of the box-and-whisker plots is depicted below. White horizontal lines indicate medians. X depicts mean values. Top and bottom of each box represent Q3 and Q2, respectively. Upper and lower vertical bars represent Q4 and Q1, respectively; horizontal segments on each end of the vertical bars represent minimum and maximum values. Outliers for eosinophil counts $1.501 \times 10^9/L$ to $5.0 \times 10^9/L$ and $> 5.0 \times 10^9/L$ are presented as light red and dark red dots, respectively. (c) Proportion of patients with eosinophilia grades 1–3; patient numbers are provided in Table 1c. Eosinophilia grade scale follows the guidance provided by the US FDA.³⁷ BL, baseline; *n*, number of patients; Q, quartile; qw, once weekly; q2w, every 2 weeks; SE, standard error; TCS, topical corticosteroids; Wk, week.

Fig 5. (a) Mean change in LDH from baseline to week 16 (SOLO 1 & 2) and week 52 (CHRONOS). (b) Absolute LDH levels. White horizontal lines indicate medians. X depicts mean values. Top and bottom of each box represent Q3 and Q2, respectively. Upper and lower vertical bars represent Q4 and Q1, respectively; horizontal segments on each end of the vertical bars represent minimum and maximum values. (c) Proportion of patients with shifts from high to normal values from baseline to week 16 (SOLO 1 & 2) and week 52 (CHRONOS). Normal range: 135–330 IU/L (female) and 135–281 IU/L (male) in SOLO 1 & 2, respectively and 53–234 IU/L in CHRONOS. BL, baseline; LDH, lactate dehydrogenase; *n*, number of patients; *N1*, total number of patients with at least one value at visit; Q, quartile; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids; Wk, week.



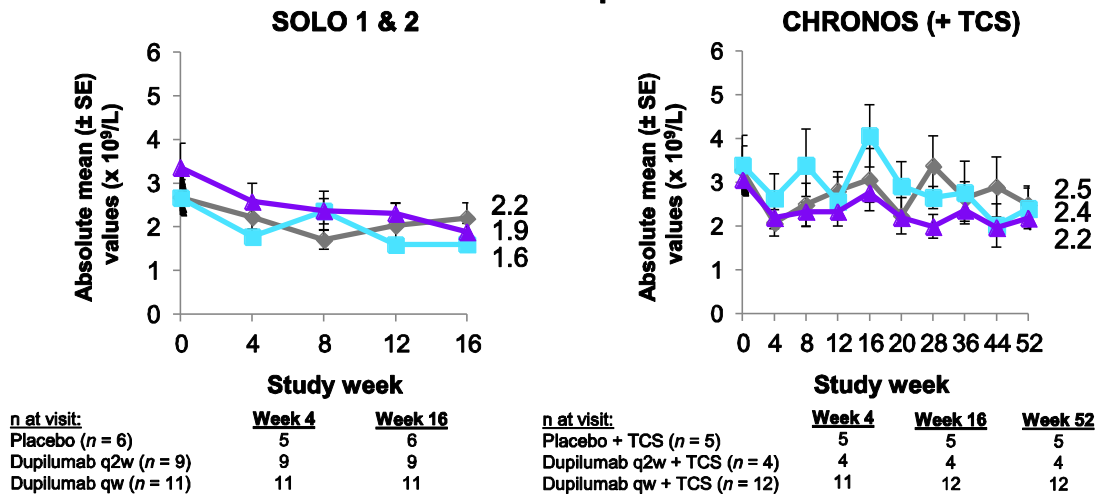
(a)

Platelets



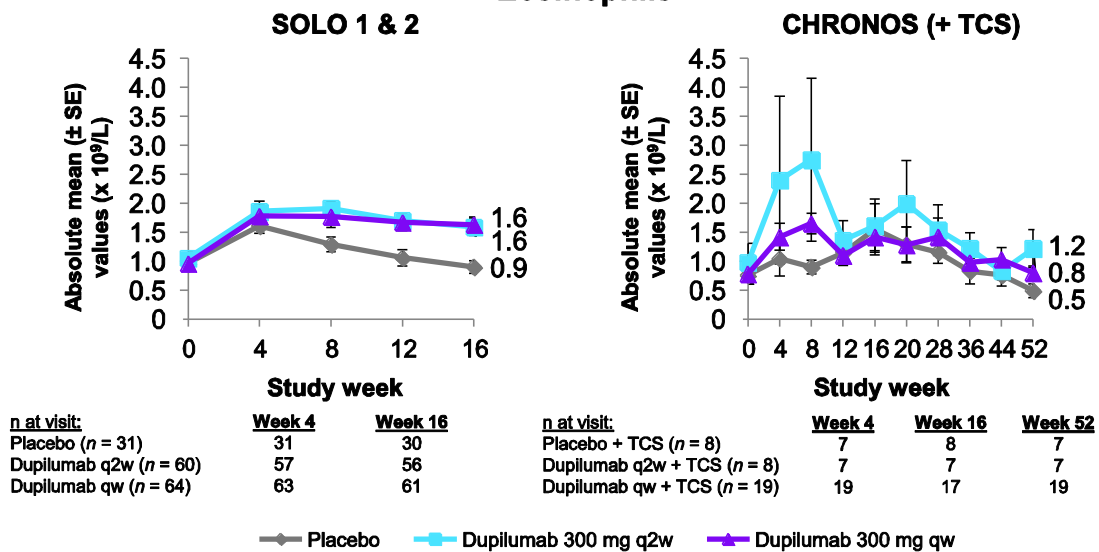
(b)

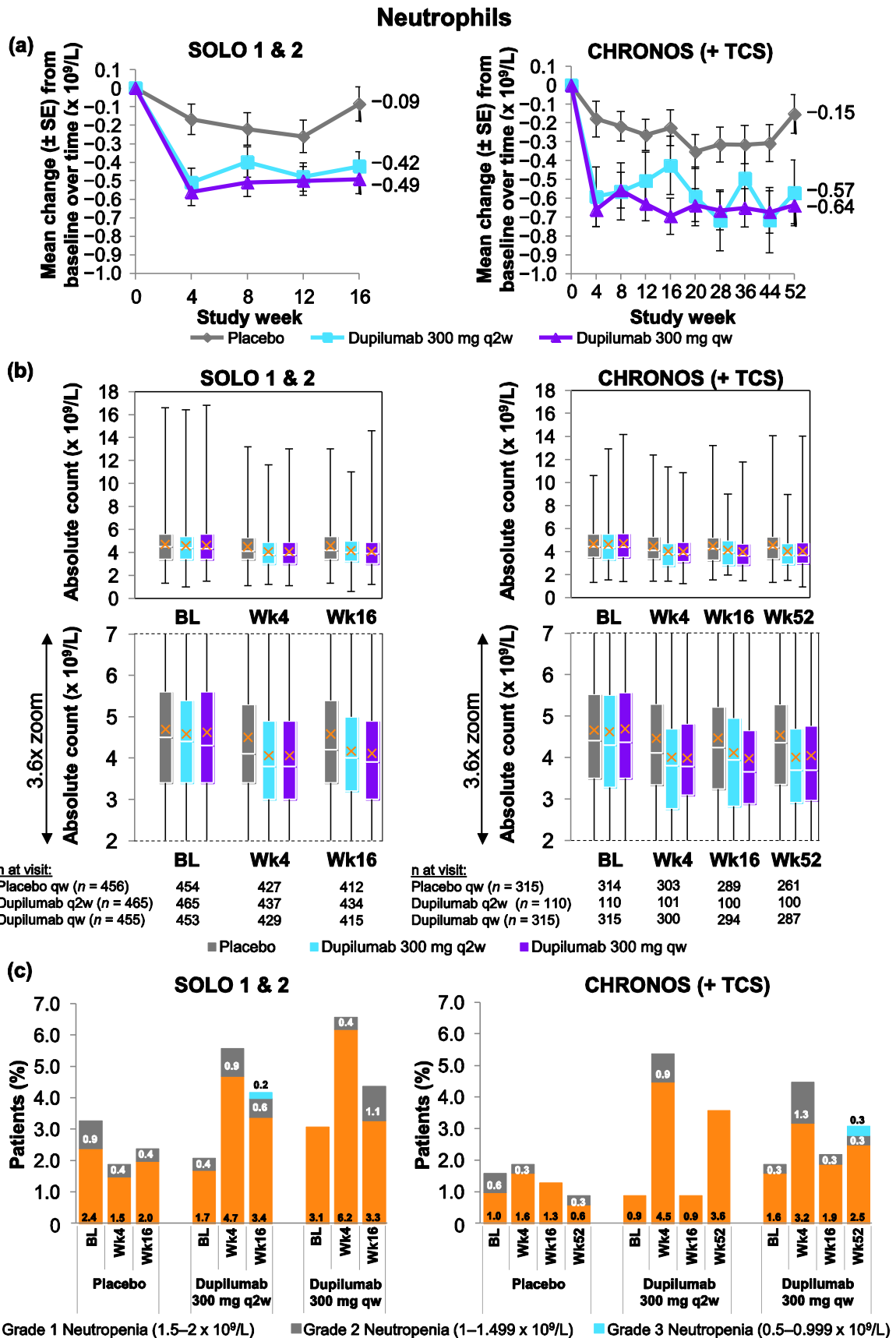
Neutrophils

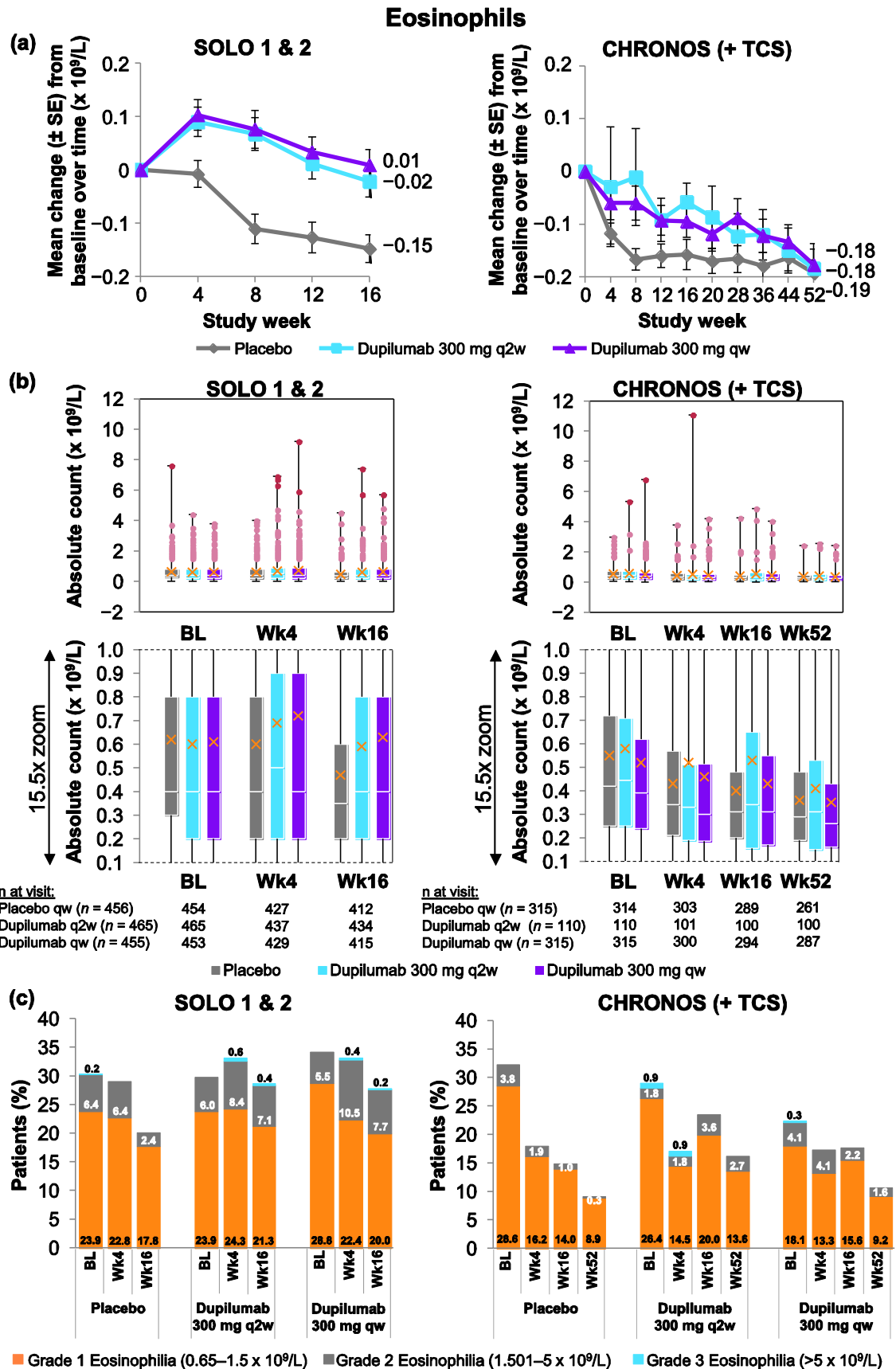


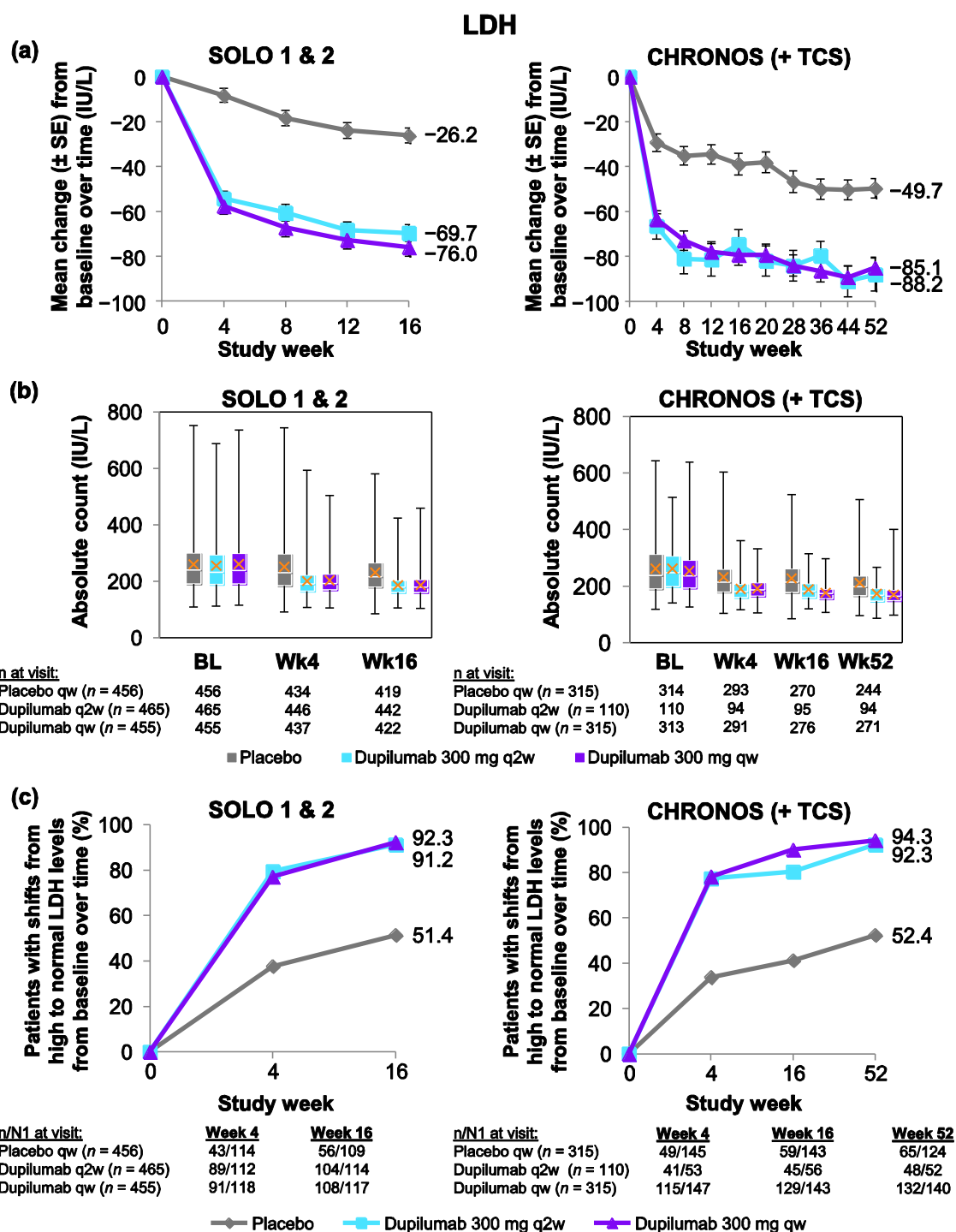
(c)

Eosinophils

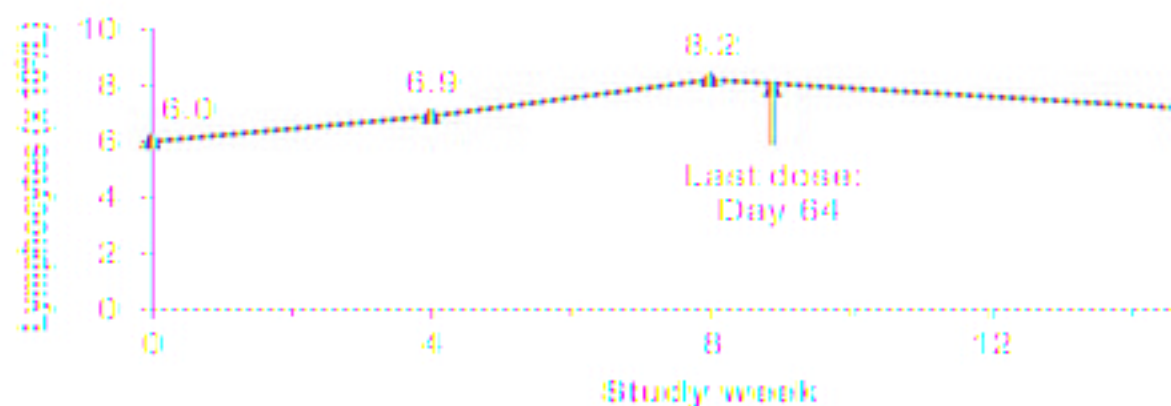




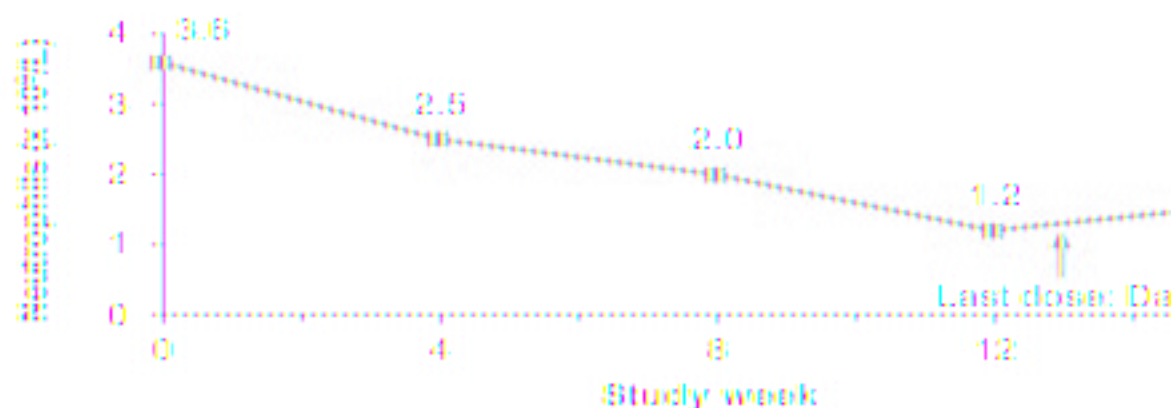




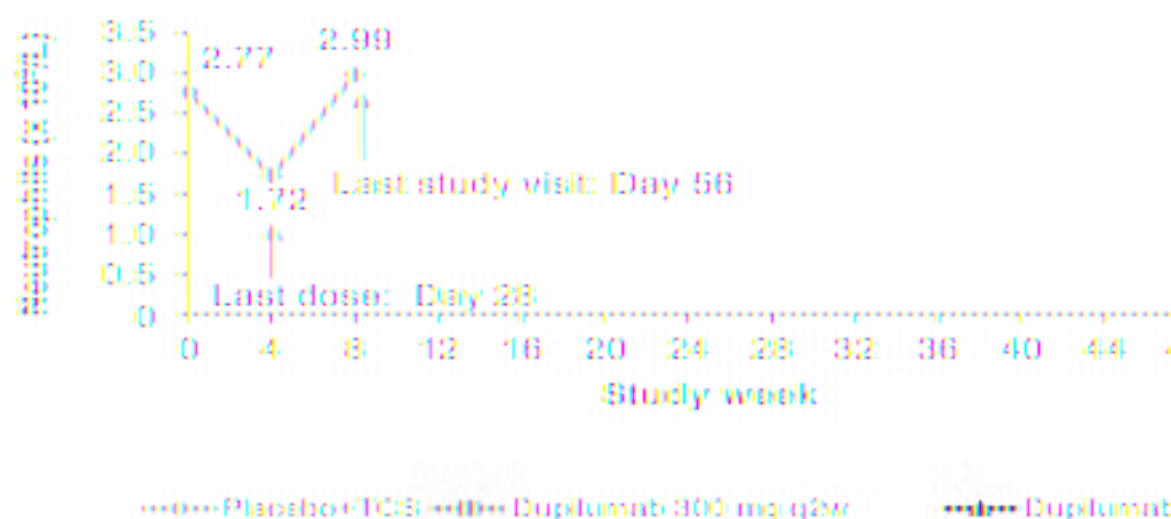
(a)



(b)



(c)



Supporting information to:

Laboratory safety of dupilumab in moderate-to-severe atopic dermatitis: results from

three phase III trials

(LIBERTY AD SOLO 1, LIBERTY AD SOLO 2, LIBERTY AD CHRONOS)

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Supplemental Table S5. Adverse events (based on MedDRA-Preferred Term) in dupilumab-treated patients^a with an eosinophil count $> 5.0 \times 10^9/\text{L}$ at any visit in SOLO 1 & 2 and CHRONOS

Supplemental Table S6a. Summary statistics for haematology laboratory parameters in patients who discontinued study treatment due to haematological TEAEs or any TEAE: red blood cells and platelets. Values that are noticeably higher or lower than the overall population are highlighted in yellow.

Supplemental Table S6b. Summary statistics for haematology laboratory parameters in patients who discontinued study treatment due to haematological TEAEs or any TEAE: white blood cells. Values that are noticeably higher or lower than the overall population are highlighted in yellow.

Supplemental Fig. S1. Haematological data over time in patients who withdrew due to haematological adverse events.

Reference

Supplemental Table S1a. Summary statistics for haematology laboratory parameters: red blood cells and platelets

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
Haematocrit (ratio)	NR	Female: 0.3–0.5 Male: 0.4–0.5			Female: 0.3–0.5 Male: 0.4–0.5		
	BL	0.4 (0.4, 0.5), 455	0.4 (0.4, 0.5), 465	0.4 (0.4, 0.5), 453	0.4 (0.4, 0.5), 314	0.4 (0.4, 0.5), 110	0.4 (0.4, 0.5), 315
	4	0.4 (0.4, 0.5), 429	0.4 (0.4, 0.5), 437	0.4 (0.4, 0.5), 430	0.4 (0.4, 0.5), 300	0.4 (0.4, 0.5), 101	0.4 (0.4, 0.5), 294
	16	0.4 (0.4, 0.5), 414	0.4 (0.4, 0.5), 434	0.4 (0.4, 0.5), 416	0.4 (0.4, 0.5), 289	0.4 (0.4, 0.5), 100	0.4 (0.4, 0.5), 292
		−0.0 (0.2), 413	−0.0 (0.3), 434	−0.0 (0.3), 414	0.0 (0.0), 288	0.0 (0.0), 100	0.0 (0.0), 292
	52	n/a	n/a	n/a	0.4 (0.4, 0.5), 261	0.4 (0.4, 0.5), 100	0.4 (0.4, 0.5), 284

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>							
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0.0 (0.0), 260	−0.0 (0.0), 100	−0.0 (0.0), 284
Haemoglobin (g/L)	NR	Female: 110.0–155.0 Male: 125.0–170.0			Female: 115.0–164.0 Male: 125.0–181.0		
	BL	142.0 (133.0, 152.0), 455	144.0 (134.0, 154.0), 465	145.0 (134.0, 154.0), 453	146.0 (135.0, 154.0), 314	143.5 (135.0, 151.0), 110	145.0 (136.0, 154.0), 315
	4	139.0 (131.0, 150.0), 429	142.0 (131.0, 151.0), 437	144.0 (132.0, 153.0), 430	144.0 (134.0, 153.0), 303	143.0 (134.0, 152.0), 101	144.0 (135.0, 153.0), 300
	16	141.5 (130.0, 150.0), 414	143.0 (131.0, 153.0), 434	143.0 (132.0, 153.0), 416	145.0 (134.0, 153.0), 289	144.0 (134.5, 154.0), 100	145.0 (134.0, 154.0), 294
		−1.9 (7.6), 413	−1.4 (8.2), 434	−1.7 (7.7), 414	−0.9 (8.1), 288	0.1 (7.4), 100	−1.3 (8.2), 294
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	145.0 (136.0, 152.0), 261	144.5 (133.0, 154.0), 100	145.0 (135.0, 154.0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>							
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0.3 (8.6), 260	−0.3 (8.5), 100	−1.2 (8.6), 287
Erythrocyte mean corpuscular haemoglobin (pg)	NR	27.0–34.0			26.0–34.0		
	BL	30.2 (29.1, 31.3), 455	30.3 (29.3, 31.3), 465	30.2 (29.2, 31.2), 453	30.0 (29.0, 32.0), 314	30.5 (29.0, 32.0), 110	30.0 (29.0, 31.0), 315
	4	30.1 (29.0, 31.1), 429	30.3 (29.3, 31.2), 437	30.1 (29.0, 31.2), 430	30.0 (29.0, 32.0), 303	31.0 (29.0, 31.0), 101	30.0 (29.0, 31.0), 300
	16	29.8 (28.8, 30.7), 414	29.9 (28.9, 30.9), 434	29.9 (28.7, 31.0), 416	30.0 (29.0, 31.0), 289	30.0 (29.0, 31.0), 100	30.0 (29.0, 31.0), 294
		−0.4 (0.9), 413	−0.4 (0.8), 434	−0.4 (0.8), 414	−0.1 (1.0), 288	−0.3 (1.0), 100	−0.1 (0.9), 294
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	30.0 (29.0, 31.0), 261	30.0 (29.0, 31.0), 100	30.0 (29.0, 31.0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1							
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-0.2 (1.1), 260	-0.4 (1.3), 100	-0.3 (1.0), 287
Erythrocyte mean corpuscular haemoglobin concentration (g/L)	NR	310.0–360.0			310.0–380.0		
	BL	323.0 (317.0, 329.0), 455	323.0 (317.0, 329.0), 465	323.0 (316.0, 329.0), 453	339.0 (330.0, 347.0), 314	340.0 (330.0, 350.0), 110	340.0 (330.0, 347.0), 315
	4	321.0 (313.0, 327.0), 429	321.0 (315.0, 329.0), 437	321.0 (314.0, 328.0), 430	340.0 (330.0, 347.5), 300	340.0 (330.0, 346.0), 101	340.0 (330.0, 348.0), 294
	16	321.0 (315.0, 327.0), 414	322.0 (318.0, 328.0), 434	322.0 (316.0, 328.0), 416	335.0 (325.0, 341.0), 289	334.5 (324.5, 341.0), 100	336.0 (330.0, 341.0), 292
		-0.1 (1.0), 413	-0.1 (1.0), 434	-0.0 (1.0), 414	-4.6 (12.6), 288	-5.2 (14.4), 100	-3.1 (12.4), 292
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	340.0 (330.0, 350.0), 261	340.0 (330.0, 350.0), 100	340.0 (330.0, 350.0), 284

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·3 (12·8), 260	0·5 (11·3), 100	1·5 (11·6), 284
Erythrocyte mean corpuscular volume (fL)	NR	Female: 82·0–102·0 Male: 78·0–100·0			79·0–100·0		
	BL	93·6 (90·1, 97·0), 455	93·7 (90·4, 96·8), 465	93·4 (90·2, 96·9), 453	90·0 (86·0, 93·0), 314	89·0 (86·0, 94·0), 110	89·0 (86·0, 93·0), 315
	4	93·8 (90·4, 97·4), 429	93·7 (90·7, 96·9), 437	93·8 (90·2, 97·3), 430	89·5 (86·0, 92·0), 300	89·0 (86·0, 93·0), 101	89·0 (87·0, 92·0), 294
	16	92·6 (89·5, 95·9), 414	92·9 (89·8, 95·7), 434	92·7 (89·3, 96·3), 416	91·0 (88·0, 94·0), 289	90·0 (87·0, 94·0), 100	90·0 (87·0, 93·0), 292
		−1·0 (2·5), 413	−1·1 (2·7), 434	−1·1 (2·7), 414	0·9 (3·4), 288	0·5 (3·5), 100	0·5 (3·2), 292
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	89·0 (86·0, 92·0), 261	89·0 (86·0, 92·0), 100	88·0 (85·0, 91·0), 284

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-0.7 (3.1), 260	-1.1 (3.8), 100	-1.2 (3.1), 284
Platelets (10 ⁹ /L)	NR	125.0–375.0			130.0–400.0		
	BL	265.0 (229.0, 306.0), 451	259.0 (226.0, 305.0), 464	261.0 (224.0, 304.0), 450	270.0 (224.0, 313.0), 313	273.5 (239.0, 332.0), 110	266.5 (228.0, 314.0), 314
	4	268.0 (228.0, 308.0), 423	255.0 (220.0, 298.5), 424	254.0 (217.0, 293.0), 423	262.0 (218.0, 309.0), 301	264.0 (219.5, 306.0), 100	254.0 (215.0, 294.0), 298
	16	259.5 (220.5, 304.0), 404	252.0 (223.5, 297.5), 428	249.5 (215.0, 288.0), 414	253.0 (214.0, 298.0), 287	253.0 (213.5, 295.5), 100	243.0 (209.0, 283.0), 293
		-3.1 (45.0), 400	-5.7 (42.3), 428	-11.2 (36.8), 410	-14.7 (45.3), 286	-23.3 (52.5), 100	-27.7 (56.5), 292
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	267.5 (230.5, 312.0), 260	262.0 (224.0, 310.0), 99	254.0 (223.0, 303.0), 286

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-2.2 (42.8), 259	-12.9 (58.1), 99	-13.1 (51.0), 285
Erythrocytes (10 ¹² /L)	NR	Female: 3.7–5.2 Male: 4.0–5.6			Female: 3.9–5.6 Male: 4.0–6.4		
	BL	4.7 (4.4, 5.1), 455	4.8 (4.4, 5.1), 465	4.8 (4.4, 5.1), 453	4.8 (4.5, 5.1), 314	4.7 (4.4, 5.0), 110	4.8 (4.5, 5.1), 315
	4	4.7 (4.3, 5.0), 429	4.7 (4.4, 5.0), 437	4.8 (4.4, 5.1), 430	4.8 (4.5, 5.0), 303	4.8 (4.4, 5.0), 101	4.8 (4.5, 5.0), 300
	16	4.7 (4.4, 5.1), 414	4.8 (4.4, 5.1), 434	4.8 (4.4, 5.1), 416	4.8 (4.5, 5.0), 289	4.8 (4.4, 5.1), 100	4.8 (4.5, 5.1), 294
		0.0 (0.3), 413	0.0 (0.3), 434	0.0 (0.3), 414	-0.1 (0.3), 288	0.0 (0.2), 100	-0.0 (0.3), 294
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	4.8 (4.5, 5.1), 261	4.8 (4.4, 5.1), 100	4.8 (4.5, 5.2), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>							
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·0 (0·3), 260	0·0 (0·3), 100	0·0 (0·3), 287

BL, baseline; *n*, total number of patients in the treatment group; *n1*, number of patients at visit; *n/a*, not applicable; NR, normal range; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids.

Supplemental Table S1b. Summary statistics for haematology laboratory parameters: white blood cells

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>							
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Basophils (10 ⁹ /L)	NR	0·0–0·3			0·0–0·2		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	0.0 (0.0, 0.0), 454	0.0 (0.0, 0.0), 465	0.0 (0.0, 0.0), 453	0.0 (0.0, 0.01), 314	0.0 (0.0, 0.1), 110	0.0 (0.0, 0.1), 315
	4	0.0 (0.0, 0.0), 427	0.0 (0.0, 0.0), 437	0.0 (0.0, 0.0), 429	0.0 (0.0, 0.1), 303	0.0 (0.0, 0.1), 101	0.0 (0.0, 0.1), 300
	16	0.0 (0.0, 0.0), 412	0.0 (0.0, 0.0), 434	0.0 (0.0, 0.0), 415	0.0 (0.0, 0.1), 289	0.1 (0.0, 0.1), 100	0.0 (0.0, 0.1), 294
		0.0 (0.0), 411	0.0 (0.0), 434	-0.0 (0.0), 413	-0.0 (0.0), 288	0.0 (0.0), 100	0.0 (0.0), 294
	52	n/a	n/a	n/a	0.0 (0.0, 0.1), 261	0.0 (0.0, 0.1), 100	0.0 (0.0, 0.1), 287
		n/a	n/a	n/a	-0.0 (0.0), 260	-0.0 (0.1), 100	-0.0 (0.0), 287
Basophils/ leukocytes (%)	NR	0.0–3.0			0.0–2.0		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	0·3 (0·2, 0·5), 454	0·3 (0·2, 0·5), 465	0·3 (0·2, 0·5), 453	0·6 (0·4, 0·9), 314	0·7 (0·5, 0·9), 110	0·6 (0·5, 0·8), 315
	4	0·3 (0·2, 0·5), 427	0·4 (0·2, 0·6), 437	0·4 (0·2, 0·5), 429	0·6 (0·4, 0·8), 303	0·7 (0·5, 0·9), 101	0·6 (0·5, 0·9), 300
	16	0·3 (0·2, 0·5), 412	0·4 (0·2, 0·5), 434	0·4 (0·2, 0·5), 415	0·6 (0·5, 0·9), 289	0·8 (0·6, 1·1), 100	0·7 (0·5, 1·0), 294
		0·1 (0·4), 411	0·1 (0·4), 434	0·1 (0·5), 413	0·0 (0·5), 288	0·1 (0·7), 100	0·1 (0·5), 294
	52	n/a	n/a	n/a	0·6 (0·5, 0·9), 261	0·7 (0·5, 0·9), 100	0·6 (0·5, 0·9), 287
		n/a	n/a	n/a	0·0 (0·5), 260	-0·0 (0·8), 100	0·0 (0·5), 287
Eosinophils (10 ⁹ /L)	NR	0·0–0·8			0·0–0·6		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	0·4 (0·3, 0·8), 454	0·4 (0·2, 0·8), 465	0·4 (0·2, 0·8), 453	0·4 (0·3, 0·7), 314	0·4 (0·3, 0·7), 110	0·4 (0·2, 0·6), 315
	4	0·4 (0·2, 0·8), 427	0·5 (0·2, 0·9), 437	0·4 (0·2, 0·9), 429	0·3 (0·2, 0·6), 303	0·3 (0·2, 0·5), 101	0·3 (0·2, 0·5), 300
	16	0·4 (0·2, 0·6), 412	0·4 (0·2, 0·8), 434	0·4 (0·2, 0·8), 415	0·3 (0·2, 0·5), 289	0·3 (0·2, 0·7), 100	0·3 (0·2, 0·6), 294
		−0·2 (0·5), 411	−0·0 (0·6), 434	−0·0 (0·6), 413	−0·2 (0·5), 288	−0·1 (0·4), 100	−0·1 (0·5), 294
	52	n/a	n/a	n/a	0·3 (0·2, 0·5), 261	0·3 (0·2, 0·5), 100	0·3 (0·2, 0·4), 287
		n/a	n/a	n/a	−0·2 (0·4), 260	−0·2 (0·5), 100	−0·2 (0·5), 287
Eosinophils/ leukocytes (%)	NR	0·0–7·0			0·0–6·8		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	6·3 (3·6, 10·3), 454	6·4 (3·5, 10·8), 465	6·4 (3·4, 10·6), 453	6·4 (3·7, 9·5), 314	6·7 (3·6, 9·6), 110	5·6 (3·8, 8·2), 315
	4	6·1 (3·4, 10·4), 427	7·1 (3·4, 12·7), 437	6·4 (3·3, 13·1), 429	5·1 (3·2, 8·3), 303	5·5 (3·1, 8·4), 101	4·8 (3·1, 8·0), 300
	16	4·8 (2·3, 9·1), 412	5·7 (2·5, 10·9), 434	6·4 (3·1, 11·8), 415	4·8 (3·0, 7·2), 289	5·8 (2·9, 8·9), 100	4·8 (2·9, 8·8), 294
		−1·5 (5·1), 411	0·0 (6·0), 434	0·5 (6·4), 413	−1·7 (5·3), 288	−0·8 (4·6), 100	−0·6 (5·1), 294
	52	n/a	n/a	n/a	4·4 (2·9, 6·8), 261	4·8 (2·6, 8·0), 100	4·1 (2·6, 6·7), 287
		n/a	n/a	n/a	−2·1 (4·5), 260	−2·0 (4·7), 100	−1·6 (4·7), 287
Lymphocytes (10 ⁹ /L)	NR	0·9–3·6			0·8–4·3		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	1·6 (1·3, 2·0), 454	1·6 (1·3, 2·1), 465	1·7 (1·3, 2·1), 453	1·5 (1·2, 1·8), 314	1·4 (1·2, 1·8), 110	1·5 (1·2, 1·9), 315
	4	1·7 (1·4, 2·1), 427	1·8 (1·5, 2·2), 437	1·8 (1·5, 2·2), 429	1·5 (1·2, 1·9), 303	1·6 (1·2, 1·9), 101	1·6 (1·3, 2·0), 300
	16	1·7 (1·3, 2·1), 412	1·8 (1·4, 2·2), 434	1·8 (1·4, 2·2), 415	1·5 (1·2, 2·0), 289	1·5 (1·3, 1·9), 100	1·6 (1·3, 2·0), 294
		−0·0 (0·6), 411	0·1 (0·6), 434	0·1 (0·7), 413	0·1 (0·4), 288	0·2 (0·4), 100	0·1 (0·5), 294
	52	n/a	n/a	n/a	1·5 (1·2, 1·9), 261	1·7 (1·3, 2·1), 100	1·7 (1·4, 2·0), 287
		n/a	n/a	n/a	0·1 (0·5), 260	0·2 (0·4), 100	0·1 (0·5), 287
Lymphocytes/ leukocytes (%)	NR	12·0–46·0			15·4–48·5		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	23·1 (17·8, 29·2), 454	23·5 (19·0, 28·6), 465	23·4 (19·1, 29·8), 453	21·8 (17·4, 26·3), 314	21·1 (17·8, 25·0), 110	21·9 (17·2, 27·8), 315
	4	24·4 (19·6, 30·3), 427	26·7 (22·0, 32·0), 437	26·7 (21·7, 32·7), 429	24·1 (19·0, 28·7), 303	24·9 (21·1, 30·0), 101	26·0 (21·5, 30·7), 300
	16	24·2 (19·6, 29·5), 412	26·1 (21·8, 31·4), 434	26·3 (21·7, 33·4), 415	23·2 (19·4, 28·4), 289	24·9 (20·1, 29·0), 100	26·1 (21·6, 31·2), 294
		0·6 (8·1), 411	2·4 (8·4), 434	2·7 (8·4), 413	1·8 (6·4), 288	3·2 (6·6), 100	3·8 (6·9), 294
	52	n/a	n/a	n/a	23·0 (18·9, 28·7), 261	25·4 (21·8, 32·3), 100	27·0 (22·2, 32·5), 287
		n/a	n/a	n/a	1·9 (7·0), 260	5·1 (7·2), 100	4·5 (7·4), 287
Monocytes (10 ⁹ /L)	NR	0·0–1·2			0·1–0·9		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	0·4 (0·3, 0·6), 454	0·4 (0·3, 0·5), 465	0·4 (0·3, 0·5), 453	0·4 (0·3, 0·5), 314	0·4 (0·3, 0·5), 110	0·4 (0·3, 0·5), 315
	4	0·4 (0·3, 0·5), 427	0·4 (0·3, 0·5), 437	0·4 (0·3, 0·5), 429	0·4 (0·3, 0·5), 303	0·4 (0·3, 0·5), 101	0·4 (0·3, 0·5), 300
	16	0·4 (0·3, 0·5), 412	0·4 (0·3, 0·5), 434	0·4 (0·3, 0·5), 415	0·4 (0·3, 0·5), 289	0·4 (0·3, 0·5), 100	0·4 (0·3, 0·5), 294
		−0·0 (0·2), 411	−0·0 (0·2), 434	−0·0 (0·2), 413	−0·0 (0·1), 288	−0·0 (0·1), 100	−0·0 (0·1), 294
	52	n/a	n/a	n/a	0·4 (0·3, 0·5), 261	0·4 (0·3, 0·5), 100	0·4 (0·3, 0·5), 287
		n/a	n/a	n/a	−0·0 (0·1), 260	−0·0 (0·1), 100	−0·1 (0·1), 287
Monocytes/ leukocytes (%)	NR	0·0–11·0			2·6–10·1		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	6·0 (4·3, 7·5), 454	5·8 (4·4, 7·4), 465	5·9 (4·3, 7·5), 453	5·8 (4·9, 7·1), 314	5·9 (5·0, 7·3), 110	5·8 (4·9, 6·9), 315
	4	5·8 (4·4, 7·6), 427	5·7 (4·3, 7·2), 437	5·6 (4·3, 7·4), 429	6·0 (5·0, 7·1), 303	6·1 (5·2, 7·2), 101	5·8 (5·0, 7·0), 300
	16	5·7 (4·1, 7·4), 412	5·8 (4·3, 7·3), 434	5·6 (4·2, 7·3), 415	6·2 (5·1, 7·3), 289	6·1 (4·9, 7·2), 100	5·8 (4·7, 7·0), 294
		−0·1 (2·5), 411	0·1 (2·4), 434	−0·2 (2·4), 413	0·3 (1·7), 288	−0·2 (1·7), 100	0·0 (1·7), 294
	52	n/a	n/a	n/a	5·9 (5·1, 7·0), 261	6·1 (4·8, 7·2), 100	5·6 (4·8, 6·8), 287
		n/a	n/a	n/a	−0·1 (1·8), 260	−0·2 (1·8), 100	−0·1 (1·7), 287
Neutrophils (10 ⁹ /L)	NR	1·7–7·9			2·0–7·2		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	4.5 (3.4, 5.6), 454	4.4 (3.4, 5.4), 465	4.3 (3.4, 5.6), 453	4.4 (3.5, 5.5), 314	4.3 (3.3, 5.5), 110	4.4 (3.5, 5.6), 315
	4	4.1 (3.4, 5.3), 427	3.8 (3.0, 4.9), 437	3.8 (3.0, 4.9), 429	4.1 (3.3, 5.3), 303	3.8 (2.8, 4.7), 101	3.8 (3.1, 4.8), 300
	16	4.2 (3.4, 5.4), 412	4.0 (3.2, 5.0), 434	3.9 (3.0, 4.9), 415	4.2 (3.2, 5.2), 289	3.9 (2.8, 5.0), 100	3.7 (2.9, 4.7), 294
		-0.1 (1.8), 411	-0.4 (1.6), 434	-0.5 (1.6), 413	-0.2 (1.6), 288	-0.4 (1.5), 100	-0.7 (1.7), 294
	52	n/a	n/a	n/a	4.4 (3.4, 5.3), 261	3.7 (2.9, 4.7), 100	3.7 (3.0, 4.8), 287
		n/a	n/a	n/a	-0.2 (1.6), 260	-0.6 (1.8), 100	-0.6 (1.6), 287
Neutrophils/ leukocytes (%)	NR	46.0–72.0			40.5–75.0		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	61·8 (54·7, 68·8), 454	62·0 (55·1, 68·3), 465	61·5 (54·7, 67·7), 453	64·3 (58·0, 69·4), 314	63·9 (58·8, 69·2), 110	64·4 (58·3, 69·5), 315
	4	60·7 (54·3, 66·5), 427	57·5 (50·6, 64·2), 437	57·5 (49·2, 64·8), 429	62·5 (56·4, 67·9), 303	61·9 (55·4, 65·8), 101	60·7 (54·6, 66·0), 300
	16	62·6 (56·4, 68·5), 412	59·1 (53·1, 65·3), 434	57·6 (51·8, 64·5), 415	63·4 (57·6, 68·9), 289	62·0 (55·7, 66·7), 100	60·4 (54·0, 66·2), 294
		1·0 (9·6), 411	−2·5 (9·3), 434	−3·1 (11·0), 413	−0·4 (8·1), 288	−2·4 (8·4), 100	−3·4 (8·4), 294
	52	n/a	n/a	n/a	64·1 (58·6, 69·9), 261	60·6 (55·5, 66·9), 100	60·9 (55·0, 66·7), 287
		n/a	n/a	n/a	0·3 (8·9), 260	−3·0 (9·3), 100	−2·9 (8·8), 287
Leukocytes (10 ⁹ /L)	NR	3·7–11·0			3·8–10·7		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
	BL	7.2 (5.9, 8.7), 455	7.1 (5.9, 8.5), 465	7.2 (5.9, 8.8), 453	7.1 (5.8, 8.4), 314	7.0 (5.4, 8.2), 110	7.0 (5.8, 8.4), 315
	4	6.9 (6.0, 8.5), 429	6.7 (5.7, 8.1), 437	6.7 (5.7, 8.3), 430	6.6 (5.6, 7.9), 303	6.0 (4.9, 7.4), 101	6.4 (5.2, 7.7), 300
	16	6.9 (5.8, 8.2), 414	6.8 (5.8, 8.1), 434	6.8 (5.6, 8.1), 416	6.8 (5.4, 8.1), 289	6.4 (5.2, 8.0), 100	6.1 (5.1, 7.7), 294
		-0.3 (2.1), 413	-0.4 (2.0), 434	-0.4 (1.8), 414	-0.3 (1.8), 288	-0.4 (1.7), 100	-0.7 (1.9), 294
	52	n/a	n/a	n/a	6.9 (5.7, 7.9), 261	6.2 (5.2, 7.7), 100	6.1 (5.3, 7.5), 287
		n/a	n/a	n/a	-0.3 (1.9), 260	-0.6 (1.9), 100	-0.7 (1.9), 287

BL, baseline; *n*, total number of patients in the treatment group; *n1*, number of patients at visit; n/a, not applicable; NR, normal range; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids.

Supplemental Table S2a. Summary statistics for serum chemistry laboratory parameters: metabolic function

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
Albumin (g/L)	NR	35.0–55.0			30.0–49.0		
	BL	46.0 (43.5, 48.0), 456	45.0 (43.0, 48.0), 465	46.0 (44.0, 48.0), 455	43.0 (42.0, 45.0), 315	43.0 (41.0, 46.0), 110	43.0 (41.0, 46.0), 315
	4	45.0 (43.0, 47.0), 434	45.0 (43.0, 47.0), 445	46.0 (44.0, 47.0), 437	43.0 (41.0, 45.0), 309	43.0 (41.0, 45.0), 103	43.0 (41.0, 45.0), 304
	16	46.0 (43.0, 48.0), 419	46.0 (44.0, 48.0), 441	46.0 (44.0, 48.0), 421	43.0 (41.0, 45.0), 290	44.0 (41.0, 45.0), 99	43.0 (41.0, 45.0), 297
		−0.0 (3.1), 419	0.3 (3.1), 441	−0.1 (2.9), 421	−0.5 (2.9), 290	−0.3 (3.0), 99	−0.3 (3.1), 297
	52	n/a	n/a	n/a	43.0 (42.0, 45.0), 262	43.0 (41.0, 46.0), 102	43.0 (41.0, 46.0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1							
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·0 (2·9), 262	−0·2 (3·0), 102	0·1 (3·3), 287
Creatine kinase (IU/L) ^a	NR	Female: 24–169 Male: 24–207			Female: 18–169 Male: 18–198		
	BL	99·0 (74·0, 150·0), 456	99·0 (71·0, 148·0), 465	100·0 (76·0, 142·0), 455	102·0 (72·0, 143·0), 315	99·5 (76·0, 147·0), 110	102·0 (70·0, 149·0), 315
	4	98·5 (72·0, 145·0), 434	97·0 (73·0, 150·0), 445	101·0 (77·0, 150·0), 437	105·0 (74·0, 147·0), 309	103·0 (79·0, 156·0), 103	104·0 (74·5, 137·0), 304
	16	99·0 (73·0, 141·0), 419	102·0 (75·0, 151·0), 441	105·0 (75·0, 153·0), 421	104·0 (76·0, 163·0), 290	96·0 (75·0, 153·0), 99	107·0 (76·0, 162·0), 297
		−2·5 (221·1), 419	15·5 (193·4), 441	−27·0 (932·4), 421	23·1 (203·2), 290	22·7 (182·2), 99	3·5 (192·5), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	107·0 (74·0, 156·0), 261	104·5 (74·0, 152·0), 102	110·0 (74·0, 164·0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	22.9 (295.7), 261	10.2 (99.1), 102	3.1 (206.9), 287
C-reactive protein (mg/L)	NR	< 5.0			≤ 2.9		
	BL	1.5 (0.6, 3.8), 456	1.8 (0.6, 5.0), 465	1.6 (0.7, 4.5), 455	1.6 (0.7, 3.9), 313	1.9 (0.5, 5.0), 110	1.7 (0.7, 4.6), 315
	4	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>
	16	1.3 (0.5, 2.9), 418	1.1 (0.5, 3.2), 439	1.0 (0.4, 2.5), 419	1.1 (0.5, 2.9), 290	0.9 (0.3, 2.8), 102	1.0 (0.4, 2.3), 298
		-1.7 (11.0), 418	-1.7 (10.2), 439	-1.7 (8.5), 419	-1.5 (7.0), 288	-1.3 (4.9), 102	-1.7 (8.7), 298
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	1.1 (0.5, 2.9), 264	0.9 (0.3, 3.1), 102	0.9 (0.4, 2.6), 286

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0.9 (8.6), 262	−1.6 (5.5), 102	−1.4 (9.4), 286
Glucose (mmol/L)	NR	3.3–6.4			3.9–5.6		
	BL	4.9 (4.6, 5.3), 456	4.9 (4.5, 5.4), 465	4.9 (4.5, 5.4), 455	4.9 (4.6, 5.4), 315	4.9 (4.5, 5.3), 110	4.9 (4.6, 5.4), 315
	4	4.9 (4.6, 5.4), 434	5.0 (4.6, 5.4), 441	4.9 (4.6, 5.4), 434	4.9 (4.6, 5.5), 309	4.9 (4.6, 5.3), 103	5.0 (4.6, 5.3), 304
	16	4.9 (4.6, 5.4), 417	4.9 (4.5, 5.3), 438	4.9 (4.6, 5.4), 421	4.9 (4.5, 5.4), 290	5.1 (4.7, 5.5), 99	4.9 (4.6, 5.3), 296
		0.0 (1.2), 417	−0.1 (1.3), 438	0.1 (1.0), 421	0.0 (0.9), 290	0.2 (1.1), 99	0.0 (0.9), 296
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	5.1 (4.7, 5.6), 261	5.1 (4.7, 5.4), 102	5.0 (4.7, 5.4), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>							
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·2 (1·1), 261	0·2 (1·2), 102	0·1 (1·0), 287
Haemoglobin A1C (%)	NR	<i>n/a</i>			< 6·5		
	BL	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	5·4 (5·1, 5·7), 314	5·4 (5·1, 5·7), 109	5·4 (5·1, 5·6), 312
	4	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	5·9 (5·9, 5·9), 1	<i>n/a</i>	6·0 (6·0, 6·0), 1
	16	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	5·6 (4·6, 5·8), 3	5·6 (5·6, 5·6), 1	5·4 (5·2, 5·7), 3
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·0 (0·1), 3	0 (<i>n/a</i>), 1	−0·1 (0·4), 3
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	5·3 (5·2, 5·6), 263	5·4 (5·2, 5·6), 98	5·3 (5·1, 5·6), 285

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0.0 (0.3), 263	−0.0 (0.3), 98	−0.0 (0.3), 284
Protein (g/L)	NR	60.0–80.0			60.0–84.0		
	BL	73.0 (70.0, 76.0), 456	73.0 (69.0, 76.0), 465	73.0 (70.0, 76.0), 455	73.0 (70.0, 76.0), 315	73.0 (69.0, 76.0), 110	73.0 (70.0, 76.0), 315
	4	72.0 (69.0, 76.0), 434	72.0 (69.0, 75.0), 445	72.0 (70.0, 76.0), 437	73.0 (70.0, 75.0), 309	73.0 (70.0, 76.0), 103	72.0 (70.0, 75.0), 304
	16	73.0 (70.0, 77.0), 419	73.0 (70.0, 76.0), 441	73.0 (70.0, 76.0), 421	72.0 (69.0, 75.0), 290	72.0 (70.0, 75.0), 101	72.0 (69.0, 76.0), 297
		0.4 (4.7), 419	0.1 (4.8), 441	−0.3 (4.5), 421	−0.4 (4.4), 290	−0.4 (4.5), 101	−0.8 (4.4), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	73.0 (71.0, 76.0), 264	72.0 (69.0, 75.0), 102	72.0 (70.0, 76.0), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·5 (4·4), 264	−0·4 (4·7), 102	−0·2 (4·8), 288

^aCreatine kinase isoenzymes were measured when values were > 5 × ULN. *n*, total number of patients in the treatment group; *n1*, number of patients at visit; *n/a*, not applicable; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids; ULN, upper limit of normal.

Supplemental Table S2b. Summary statistics for serum chemistry laboratory parameters: electrolytes

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
Bicarbonate (mmol/L)	NR	21.0–33.0			17.0–32.0		
	BL	25.0 (23.0, 26.0), 456	25.0 (23.0, 26.0), 465	25.0 (23.0, 27.0), 455	23.9 (22.4, 25.2), 314	24.1 (22.2, 25.3), 110	23.7 (22.4, 24.9), 315
	4	25.0 (23.0, 26.0), 434	24.0 (23.0, 26.0), 445	25.0 (23.0, 27.0), 437	23.7 (22.3, 25.2), 306	23.5 (22.0, 25.1), 103	23.6 (21.9, 25.0), 303
	16	25.0 (23.0, 27.0), 419	24.0 (22.0, 27.0), 441	25.0 (23.0, 27.0), 421	23.7 (22.1, 24.9), 290	23.3 (21.5, 24.6), 98	23.4 (22.0, 24.8), 296
		−0.0 (3.7), 419	−0.2 (3.7), 441	−0.1 (3.8), 421	−0.4 (2.5), 289	−0.7 (2.5), 98	−0.4 (2.5), 296
	52	n/a	n/a	n/a	23.4 (21.8, 24.6), 262	23.5 (21.9, 25.0), 101	23.0 (21.6, 24.9), 286

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0.6 (2.4), 261	−0.6 (2.7), 101	−0.6 (2.6), 286
Calcium (mmol/L)	NR	2.1–2.6			2.1–2.6		
	BL	2.4 (2.3, 2.5), 456	2.4 (2.3, 2.4), 465	2.4 (2.3, 2.4), 455	2.4 (2.4, 2.5), 315	2.4 (2.4, 2.5), 110	2.4 (2.4, 2.5), 315
	4	2.4 (2.3, 2.4), 434	2.4 (2.3, 2.4), 444	2.4 (2.3, 2.4), 437	2.4 (2.4, 2.5), 309	2.4 (2.3, 2.5), 103	2.4 (2.4, 2.5), 304
	16	2.4 (2.3, 2.4), 419	2.4 (2.3, 2.4), 441	2.4 (2.3, 2.4), 421	2.4 (2.4, 2.5), 290	2.4 (2.3, 2.5), 101	2.4 (2.3, 2.5), 297
		−0.0 (0.1), 419	−0.0 (0.1), 441	−0.0 (0.1), 421	−0.0 (0.1), 290	−0.0 (0.1), 101	−0.0 (0.1), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	2.4 (2.4, 2.5), 264	2.4 (2.3, 2.5), 102	2.4 (2.3, 2.5), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1							
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-0.0 (0.1), 264	-0.0 (0.1), 102	-0.0 (0.1), 288
Chloride (mmol/L)	NR	95.0–110.0			94.0–112.0		
	BL	101.0 (99.0, 102.0), 456	101.0 (99.0, 103.0), 465	101.0 (99.0, 102.0), 455	101.0 (99.0, 102.0), 315	101.0 (99.0, 102.0), 110	101.0 (100.0, 103.0), 315
	4	101.0 (99.0, 102.0), 434	101.0 (99.0, 103.0), 445	101.0 (100.0, 102.0), 437	101.0 (100.0, 102.0), 308	101.0 (99.0, 103.0), 103	101.0 (100.0, 103.0), 304
	16	101.0 (99.0, 102.0), 419	101.0 (99.0, 102.0), 441	101.0 (99.0, 102.0), 421	101.0 (99.0, 103.0), 290	101.0 (99.0, 102.0), 101	101.0 (100.0, 102.0), 297
		-0.1 (2.8), 419	-0.4 (2.8), 441	-0.2 (2.5), 421	-0.1 (2.3), 290	-0.1 (2.5), 101	-0.2 (2.4), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	101.0 (99.0, 102.0), 264	101.0 (99.0, 102.0), 101	101.0 (100.0, 103.0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1							
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-0.2 (2.4), 264	0.0 (2.9), 101	0.1 (2.5), 287
Potassium (mmol/L)	NR	3.5–5.0			3.4–5.4		
	BL	4.2 (3.9, 4.4), 455	4.2 (4.0, 4.4), 464	4.2 (3.9, 4.4), 455	4.1 (3.9, 4.3), 315	4.0 (3.8, 4.3), 110	4.0 (3.8, 4.2), 315
	4	4.2 (4.0, 4.4), 434	4.2 (4.0, 4.4), 442	4.2 (4.0, 4.4), 437	4.0 (3.8, 4.2), 308	4.1 (3.8, 4.2), 103	4.0 (3.8, 4.2), 304
	16	4.2 (4.0, 4.4), 417	4.2 (4.0, 4.4), 440	4.2 (4.1, 4.4), 421	4.0 (3.8, 4.2), 290	4.0 (3.8, 4.2), 101	4.0 (3.8, 4.2), 296
		0.0 (0.4), 416	0.1 (0.4), 439	0.1 (0.4), 421	-0.1 (0.4), 290	-0.0 (0.4), 101	0.0 (0.4), 296
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	4.0 (3.8, 4.2), 262	4.0 (3.8, 4.2), 101	4.0 (3.8, 4.2), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0.1 (0.3), 262	−0.1 (0.4), 101	−0.0 (0.4), 287
Sodium (mmol/L)	NR	133.0–145.0			132.0–147.0		
	BL	140.0 (139.0, 142.0), 456	140.0 (139.0, 142.0), 465	140.0 (139.0, 142.0), 455	139.0 (138.0, 140.0), 315	139.0 (138.0, 141.0), 110	139.0 (138.0, 141.0), 315
	4	140.0 (139.0, 141.0), 434	140.0 (139.0, 141.0), 445	140.0 (139.0, 142.0), 437	138.0 (137.0, 140.0), 308	139.0 (137.0, 140.0), 103	138.5 (137.0, 140.0), 304
	16	140.0 (139.0, 141.0), 419	140.0 (139.0, 141.0), 441	140.0 (139.0, 141.0), 421	138.0 (137.0, 140.0), 290	138.0 (136.0, 139.0), 101	138.0 (137.0, 140.0), 297
		−0.2 (2.7), 419	−0.3 (2.5), 441	−0.3 (2.2), 421	−0.8 (2.4), 290	−1.2 (2.8), 101	−1.0 (2.3), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	138.0 (137.0, 140.0), 264	138.0 (137.0, 140.0), 101	138.0 (137.0, 139.0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-1.1 (2.4), 264	-1.0 (2.7), 101	-1.0 (2.5), 287

n, total number of patients in the treatment group; *n1*, number of patients at visit; *n/a*, not applicable; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids.

Supplemental Table S2c. Summary statistics for serum chemistry laboratory parameters: renal function

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1							
Blood urea nitrogen (mmol/L)	NR	1.8–7.1			1.4–12.1		
	BL	4.5 (3.6, 5.7), 456	4.6 (3.6, 5.7), 465	4.6 (3.6, 5.4), 455	4.6 (3.7, 5.7), 315	4.8 (3.8, 5.7), 110	4.6 (3.9, 5.7), 315
	4	4.6 (3.6, 5.4), 434	4.6 (3.9, 5.4), 445	4.6 (3.9, 5.4), 437	4.6 (3.9, 5.7), 309	4.9 (4.1, 5.7), 103	5.0 (4.0, 5.7), 304
	16	4.6 (3.6, 5.4), 419	4.6 (3.6, 5.4), 441	4.6 (3.9, 5.4), 421	4.7 (3.9, 5.7), 290	4.8 (3.9, 6.0), 101	4.9 (3.9, 5.8), 297
		−0.0 (1.3), 419	−0.0 (1.4), 441	0.1 (1.3), 421	0.1 (1.3), 290	0.2 (1.3), 101	0.1 (1.3), 297
	52	n/a	n/a	n/a	4.7 (4.0, 5.8), 264	4.7 (3.9, 5.6), 102	4.8 (4.1, 5.7), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1							
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·1 (1·2), 264	0·1 (1·2), 102	0·0 (1·2), 288
Creatinine (μ mol/L)	NR	62·0–124·0			Female: 31·0–128·0 Male: 40·0–145·0		
	BL	62·0 (53·0, 71·0), 456	62·0 (53·0, 71·0), 465	71·0 (53·0, 80·0), 455	73·0 (62·0, 86·0), 315	71·0 (62·0, 80·0), 110	73·0 (63·0, 83·0), 315
	4	62·0 (53·0, 71·0), 434	71·0 (53·0, 71·0), 446	71·0 (53·0, 80·0), 437	72·0 (62·0, 85·0), 309	71·0 (62·0, 80·0), 103	71·0 (63·0, 82·0), 304
	16	71·0 (53·0, 71·0), 419	71·0 (62·0, 80·0), 442	71·0 (62·0, 80·0), 422	74·0 (64·0, 86·0), 290	74·0 (62·0, 83·0), 101	73·0 (63·0, 85·0), 297
		0·1 (11·5), 419	–0·1 (13·0), 442	2·5 (32·5), 422	0·9 (8·8), 290	0·4 (9·3), 101	0·2 (9·0), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	75·0 (63·0, 86·5), 264	71·0 (64·0, 80·0), 102	74·0 (63·5, 86·0), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0.4 (10.3), 264	−0.4 (10.4), 102	0.1 (9.1), 288
Urate (μmol/L)	NR	Female: 119.0–357.0 Male: 238.0–476.0			Female: 125.0–446.0 Male: 125.0–494.0		
	BL	333.0 (280.0, 410.0), 456	351.0 (286.0, 416.0), 465	351.0 (286.0, 410.0), 455	349.0 (294.0, 422.0), 315	342.0 (281.0, 393.0), 110	351.0 (280.0, 415.0), 315
	4	339.0 (280.0, 410.0), 434	357.0 (280.0, 416.0), 445	351.0 (280.0, 410.0), 437	352.0 (291.0, 419.0), 309	333.0 (271.0, 387.0), 103	333.5 (268.5, 411.0), 304
	16	339.0 (280.0, 399.0), 419	345.0 (274.0, 404.0), 441	339.0 (274.0, 404.0), 421	347.5 (296.0, 410.0), 290	321.0 (267.0, 387.0), 101	339.0 (280.0, 410.0), 297
		−3.9 (55.1), 419	−15.2 (50.8), 441	−9.4 (47.4), 421	−4.7 (49.5), 290	−11.6 (56.2), 101	−7.8 (49.1), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	351.0 (288.5, 416.0), 264	318.0 (262.0, 379.0), 102	339.0 (269.5, 406.5), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-6.3 (54.6), 264	-21.3 (52.5), 102	-12.9 (54.1), 288

n, total number of patients in the treatment group; *n1*, number of patients at visit; *n/a*, not applicable; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids.

Supplemental Table S2d. Summary statistics for serum chemistry laboratory parameters: liver function

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
Alkaline phosphatase (IU/L)	NR	Female: 30.0–115.0 Male: 43.0–115.0			Female: 31.0–135.0 Male: 31.0–131.0		
	BL	71.5 (60.0, 85.5), 456	70.0 (59.0, 85.0), 465	71.0 (61.0, 88.0), 455	73.0 (60.0, 88.0), 315	71.0 (58.0, 85.0), 110	71.0 (60.0, 85.0), 315
	4	69.0 (59.0, 84.0), 434	67.0 (56.0, 81.0), 444	68.0 (59.0, 82.0), 437	71.0 (57.0, 85.0), 309	69.0 (56.0, 83.0), 103	67.0 (56.0, 80.5), 304
	16	69.0 (58.0, 82.0), 419	68.0 (56.0, 81.0), 441	69.0 (58.0, 81.0), 421	67.5 (58.0, 82.0), 290	72.0 (58.0, 86.0), 101	66.0 (56.0, 79.0), 296
		−1.3 (12.0), 419	−3.8 (15.2), 441	−4.2 (12.6), 421	−4.3 (11.8), 290	−1.3 (11.2), 101	−4.0 (10.7), 296
	52	n/a	n/a	n/a	72.0 (59.0, 81.5), 264	67.0 (54.0, 85.0), 102	69.0 (57.0, 79.0), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-3.0 (14.3), 264	-2.0 (13.3), 102	-1.4 (13.6), 288
Alanine aminotransfer- ase (IU/L)	NR	Female: 10.0–33.0 Male: 10.0–40.0			Female: 6.0–34.0 Male: 6.0–43.0		
	BL	19.0 (14.0, 28.0), 456	20.0 (15.0, 28.0), 465	20.0 (15.0, 29.0), 455	21.0 (15.0, 30.0), 315	20.0 (15.0, 28.0), 110	20.0 (15.0, 27.0), 315
	4	19.0 (15.0, 26.0), 434	19.0 (14.0, 27.0), 445	20.0 (14.0, 28.0), 437	19.0 (15.0, 27.0), 309	18.0 (14.0, 24.0), 103	19.0 (14.0, 28.0), 304
	16	19.0 (14.0, 26.0), 418	19.0 (14.0, 27.0), 441	19.0 (14.0, 27.0), 421	19.0 (14.0, 28.0), 290	18.0 (13.0, 25.0), 99	18.0 (13.0, 26.0), 297
		-0.4 (12.2), 418	-1.2 (14.9), 441	-0.6 (16.6), 421	-2.3 (22.3), 290	-2.6 (12.2), 99	-1.4 (9.2), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	20.0 (15.0, 28.0), 262	18.0 (14.0, 27.0), 102	20.0 (14.0, 27.0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−1.3 (16.6), 262	−1.0 (14.2), 102	0.9 (13.2), 287
Aspartate aminotransfer- ase (IU/L)	NR	Female: 10.0–36.0 Male: 10.0–43.0			Female: 9.0–34.0 Male: 11.0–36.0		
	BL	22.0 (18.0, 26.0), 456	21.0 (18.0, 26.0), 465	21.0 (17.0, 28.0), 455	23.0 (19.0, 28.0), 315	23.0 (20.0, 28.0), 110	23.0 (19.0, 27.0), 315
	4	21.0 (17.0, 26.0), 434	20.0 (17.0, 25.0), 445	21.0 (17.0, 26.0), 437	21.0 (18.0, 26.0), 309	21.0 (17.0, 26.0), 103	21.0 (18.0, 25.0), 304
	16	21.0 (17.0, 25.0), 418	20.0 (17.0, 25.0), 441	20.0 (16.0, 25.0), 421	21.0 (18.0, 26.0), 290	22.0 (17.0, 25.0), 99	20.0 (17.0, 24.0), 297
		−0.6 (9.0), 418	−1.5 (10.2), 441	−1.8 (13.8), 421	−1.2 (11.8), 290	−3.5 (18.3), 99	−2.2 (6.5), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	21.0 (18.0, 25.0), 260	21.0 (17.0, 25.0), 101	19.5 (17.0, 25.0), 286

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	-1.5 (11.7), 260	-3.5 (17.8), 101	-1.6 (8.9), 286
Direct bilirubin (μmol/L) ^a	NR	0–6.8			0–7.0		
	BL	5.6 (3.4, 8.0), 22	6.2 (4.4, 7.7), 19	6.3 (3.9, 7.5), 13	6.0 (4.0, 7.0), 7	5.0 (5.0, 7.0), 7	5.0 (5.0, 6.0), 14
	4	6.4 (4.8, 7.6), 4	6.8 (4.4, 8.0), 13	6.5 (4.6, 7.7), 11	5.0 (5.0, 6.0), 5	5.0 (5.0, 6.0), 5	5.0 (4.0, 6.0), 6
	16	7.3 (6.2, 9.1), 10	6.2 (4.3, 7.9), 15	7.0 (4.6, 8.2), 12	5.0 (5.0, 6.0), 6	4.0 (4.0, 4.0), 1	5.0 (4.0, 6.0), 10
		0.5 (2.8), 7	-0.2 (2.3), 10	0.4 (1.6), 5	0.3 (1.0), 4	0.0 (0.0), 0	-0.3 (0.8), 6
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	5.0 (4.0, 5.0), 6	6.0 (5.0, 7.0), 3	5.0 (4.0, 5.0), 13

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·0 (1·4), 2	−0·7 (0·6), 3	−0·6 (0·9), 5
Bilirubin (μmol/L)	NR	≥ 18·8			3·0–21·0		
	BL	6·0 (4·4, 8·7), 456	6·3 (4·3, 9·1), 465	6·3 (4·6, 8·6), 455	7·0 (5·0, 9·0), 315	7·0 (5·0, 10·0), 110	7·0 (5·0, 10·0), 315
	4	5·8 (4·3, 8·6), 434	6·3 (4·3, 9·1), 445	6·7 (4·4, 9·4), 437	7·0 (5·0, 9·0), 309	7·0 (5·0, 10·0), 103	7·0 (5·0, 10·0), 304
	16	6·2 (4·3, 8·9), 419	6·5 (4·6, 9·7), 441	6·7 (4·6, 9·4), 421	7·0 (5·0, 9·0), 290	9·0 (5·0, 12·0), 98	7·0 (5·0, 10·0), 297
		0·1 (3·6), 419	0·5 (4·0), 441	0·4 (3·8), 421	−0·1 (4·2), 290	0·6 (5·4), 98	−0·1 (4·3), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	7·0 (5·0, 10·0), 262	7·0 (5·0, 10·0), 101	8·0 (5·0, 11·0), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·3 (4·5), 262	0·2 (4·6), 101	0·5 (4·4), 287
Indirect bilirubin (μmol/L) ^a	NR	1·7–18·8			0–21·0		
	BL	16·2 (14·0, 18·1), 18	19·2 (15·7, 20·9), 17	17·7 (16·4, 19·3), 10	24·0 (20·0, 34·0), 7	19·0 (18·0, 22·0), 7	23·0 (21·0, 24·0), 14
	4	15·7 (14·3, 22·1), 4	15·5 (14·1, 18·8), 12	16·8 (14·0, 22·9), 11	20·0 (20·0, 22·0), 5	19·0 (18·0, 22·0), 5	23·0 (19·0, 26·0), 6
	16	14·8 (12·8, 17·1), 10	20·1 (15·6, 22·4), 14	18·4 (15·2, 21·2), 12	19·0 (18·0, 21·0), 6	42·0 (42·0, 42·0), 1	20·5 (18·0, 29·0), 10
		–3·5 (6·1), 6	–0·6 (6·7), 9	4·2 (12·0), 5	–3·3 (4·0), 4	0·0 (0·0), 0	3·5 (4·9), 6
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	19·5 (19·0, 21·0), 6	19·0 (17·0, 26·0), 3	21·0 (19·0, 26·0), 13

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−9.0 (8.5), 2	−1.3 (1.5), 3	−0.6 (4.9), 5
Lactate dehydrogenase (IU/L)	NR	Female: 135.0–330.0 Male: 135.0–281.0			53.0–234.0		
	BL	240.0 (190.0, 300.5), 456	231.0 (189.0, 295.0), 465	238.0 (191.0, 299.0), 455	237.0 (190.0, 312.0), 314	247.0 (197.0, 307.0), 110	236.0 (193.0, 292.0), 313
	4	229.5 (184.0, 298.0), 434	191.0 (165.0, 222.0), 446	192.0 (169.0, 226.0), 437	214.0 (179.0, 260.0), 293	179.5 (160.0, 208.0), 94	187.0 (164.0, 212.0), 291
	16	215.0 (179.0, 265.0), 419	179.0 (160.0, 204.0), 442	179.5 (159.0, 206.0), 422	214.0 (176.0, 262.0), 270	181.0 (159.0, 209.0), 95	173.0 (155.0, 190.0), 276
		−26.2 (69.6), 419	−69.7 (78.2), 442	−76.0 (81.8), 422	−39.0 (79.9), 269	−74.8 (64.0), 95	−79.4 (77.1), 276
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	197.5 (166.5, 236.5), 244	168.0 (147.0, 192.0), 94	164.0 (149.0, 186.0), 271

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−49.7 (67.2), 243	−88.2 (72.1), 94	−85.1 (78.8), 271

^aDirect and indirect bilirubin were measured when the total bilirubin was above the ULN. *n*, total number of patients in the treatment group; *n1*, number of patients at visit; *n/a*, not applicable; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids; ULN, upper limit of normal.

Supplemental Table S2e. Summary statistics for serum chemistry laboratory parameters: lipid panel

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
Cholesterol (mmol/L)	NR	3.2–5.2			Female: 3.2–9.1 Male: 3.0–7.8		
	BL	4.8 (4.1, 5.5), 456	4.7 (4.2, 5.4), 465	4.8 (4.2, 5.5), 455	4.9 (4.2, 5.5), 315	4.8 (4.2, 5.3), 110	4.8 (4.2, 5.5), 315
	4	4.8 (4.2, 5.5), 434	4.7 (4.3, 5.4), 446	4.9 (4.2, 5.5), 437	4.9 (4.3, 5.5), 309	4.7 (4.2, 5.4), 103	4.9 (4.3, 5.6), 304
	16	4.9 (4.3, 5.6), 419	4.8 (4.2, 5.6), 442	4.9 (4.2, 5.6), 422	4.8 (4.2, 5.5), 290	4.8 (4.2, 5.4), 101	4.7 (4.2, 5.5), 297
		0.1 (0.6), 419	0.1 (0.7), 442	0.1 (0.7), 422	−0.0 (0.7), 290	0.0 (0.6), 101	0.0 (0.6), 297
	52	n/a	n/a	n/a	4.9 (4.3, 5.7), 264	4.8 (4.3, 5.4), 102	4.9 (4.2, 5.5), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>							
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·1 (0·7), 264	0·0 (0·7), 102	0·1 (0·7), 288
HDL cholesterol (mmol/L)	NR	1·0–1·6			Female: 0·9–2·5 Male: 0·7–1·9		
	BL	1·4 (1·2, 1·7), 456	1·4 (1·2, 1·7), 465	1·4 (1·1, 1·6), 455	1·4 (1·2, 1·7), 315	1·5 (1·2, 1·7), 110	1·5 (1·2, 1·8), 315
	4	1·4 (1·2, 1·7), 433	1·4 (1·2, 1·7), 444	1·4 (1·1, 1·7), 436	1·4 (1·2, 1·7), 308	1·5 (1·2, 1·8), 103	1·5 (1·2, 1·7), 304
	16	1·5 (1·2, 1·7), 419	1·4 (1·2, 1·7), 441	1·4 (1·2, 1·7), 421	1·4 (1·2, 1·7), 289	1·5 (1·2, 1·8), 101	1·5 (1·2, 1·8), 297
		0·0 (0·3), 419	0·0 (0·3), 441	0·0 (0·2), 421	0·0 (0·3), 289	0·1 (0·2), 101	0·0 (0·3), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	1·4 (1·2, 1·7), 264	1·5 (1·2, 1·7), 101	1·5 (1·2, 1·7), 287

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1							
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·0 (0·3), 264	−0·0 (0·3), 101	−0·0 (0·3), 287
LDL cholesterol (mmol/L)	NR	1·3–4·1			Female: 1·5–5·8 Male: 1·6–5·4		
	BL	2·6 (2·1, 3·2), 456	2·6 (2·2, 3·2), 465	2·7 (2·2, 3·2), 455	2·7 (2·2, 3·3), 313	2·6 (2·0, 3·1), 108	2·7 (2·1, 3·3), 312
	4	2·6 (2·2, 3·2), 433	2·6 (2·2, 3·2), 444	2·7 (2·2, 3·3), 436	2·7 (2·2, 3·4), 303	2·6 (2·2, 3·0), 100	2·7 (2·1, 3·3), 300
	16	2·7 (2·2, 3·3), 419	2·6 (2·2, 3·2), 441	2·7 (2·2, 3·3), 420	2·7 (2·1, 3·3), 283	2·5 (2·0, 3·0), 99	2·6 (2·1, 3·2), 294
		0·1 (0·5), 419	0·1 (0·6), 441	0·1 (0·5), 420	−0·0 (0·5), 281	−0·1 (0·5), 98	−0·0 (0·5), 291
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	2·8 (2·3, 3·4), 259	2·6 (2·1, 3·0), 99	2·6 (2·1, 3·2), 284

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·1 (0·6), 257	−0·0 (0·6), 98	0·0 (0·6), 281
Triglycerides (mmol/L)	NR	0·5–2·3			Female: 0·4–3·0 Male: 0·4–3·7		
	BL	1·2 (0·9, 1·8), 456	1·3 (0·9, 1·8), 465	1·3 (0·9, 1·8), 455	1·2 (0·9, 1·8), 315	1·2 (0·8, 1·7), 110	1·2 (0·8, 1·8), 315
	4	1·2 (0·9, 1·8), 434	1·3 (0·9, 2·0), 445	1·4 (1·0, 2·2), 437	1·3 (0·9, 1·8), 309	1·3 (0·8, 1·7), 103	1·2 (0·9, 1·8), 304
	16	1·2 (0·9, 1·8), 419	1·3 (1·0, 1·9), 441	1·3 (0·9, 1·9), 421	1·2 (0·9, 1·9), 290	1·3 (1·0, 1·9), 101	1·3 (0·9, 1·8), 297
		0·0 (0·9), 419	0·1 (0·9), 441	−0·0 (0·7), 421	0·1 (0·8), 290	0·1 (0·6), 101	0·1 (0·8), 297
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	1·3 (0·9, 2·0), 264	1·3 (0·9, 1·8), 102	1·3 (0·9, 1·9), 288

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	0·1 (0·8), 264	0·2 (0·9), 102	0·1 (0·8), 288

HDL, high-density lipoprotein; LDL, low-density lipoprotein; *n*, total number of patients in the treatment group; *n1*, number of patients at visit; *n/a*, not applicable; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids.

Supplemental Table S3. Summary statistics for urinalysis laboratory parameters

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n</i> 1							
Weeks 16 and 52: <i>Mean change from baseline</i> ($\pm$ SD), <i>n</i> 1							
		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
pH	NR	5.0–8.0			5.0–8.0		
	BL	6.0 (6.0, 6.5), 450	6.0 (6.0, 6.5), 460	6.0 (6.0, 6.5), 447	5.5 (5.5, 6.5), 315	5.5 (5.5, 6.5), 110	5.5 (5.5, 6.0), 315
	4	n/a	n/a	n/a	n/a	n/a	n/a
	16	6.0 (6.0, 6.5), 403	6.0 (6.0, 6.5), 431	6.0 (6.0, 6.5), 397	6.0 (5.5, 6.5), 286	5.5 (5.5, 6.0), 103	5.5 (5.5, 6.0), 291
		0.0 (0.7), 402	0.1 (0.6), 430	−0.0 (0.7), 397	0.0 (0.7), 286	0.0 (0.8), 103	0.0 (0.6), 291
	52	n/a	n/a	n/a	5.5 (5.5, 6.0), 260	6.0 (5.5, 6.3), 100	5.5 (5.5, 6.0), 286

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0·0 (0·7), 260	0·0 (0·7), 100	−0·0 (0·6), 286
Specific gravity	NR	1·00–1·04			1·00–1·04		
	BL	1·02 (1·02, 1·03), 450	1·02 (1·02, 1·03), 460	1·02 (1·02, 1·03), 447	1·02 (1·02, 1·02), 315	1·02 (1·01, 1·02), 110	1·02 (1·02, 1·02), 315
	4	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>
	16	1·02 (1·01, 1·03), 403	1·02 (1·01, 1·03), 431	1·02 (1·02, 1·03), 397	1·02 (1·01, 1·02), 286	1·02 (1·01, 1·02), 103	1·02 (1·01, 1·02), 291
		−0·00 (0·01), 402	−0·00 (0·01), 430	−0·00 (0·01), 397	−0·00 (0·01), 286	−0·00 (0·01), 103	−0·00 (0·01), 291
	52	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	1·02 (1·01, 1·02), 260	1·02 (1·01, 1·02), 100	1·02 (1·01, 1·02), 286

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
All time points: Median (Q1, Q3), <i>n1</i>							
Weeks 16 and 52: <i>Mean change from baseline (± SD), n1</i>							
		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	−0.00 (0.01), 260	−0.00 (0.01), 100	−0.00 (0.01), 286

n, total number of patients in the treatment group; *n1*, number of patients at visit; *n/a*, not applicable; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids.

Supplemental Table S4a. Shift from baseline: platelets (x 10⁹/L)

Study week	Evaluation <i>n/N1</i> (%)	SOLO 1 & 2									CHRONOS								
		Placebo qw (<i>n</i> = 456)			Dupilumab 300 mg q2w (<i>n</i> = 465)			Dupilumab 300 mg qw (<i>n</i> = 455)			Placebo qw + TCS (<i>n</i> = 315)			Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)			Dupilumab 300 mg qw + TCS (<i>n</i> = 315)		
		Baseline status																	
		L	N	H	L	N	H	L	N	H	L	N	H	L	N	H	L	N	H
4	L	1/4 (25.0)	1/392 (0.3)	0/23	3/4 (75.0)	3/398 (0.8)	0/22	2/3 (66.7)	0/389	0/30	0/1	0/286	0/13	0/1	0/91	0/8	0/1	2/280 (0.7)	0/17
	N	2/4 (50.0)	375/392 (95.7)	7/23 (30.4)	1/4 (25.0)	388/398 (97.5)	9/22 (40.9)	1/3 (33.3)	386/389 (99.2)	12/30 (40.0)	1/1 (100)	282/286 (98.6)	6/13 (46.2)	1/1 (100)	88/91 (96.7)	3/8 (37.5)	1/1 (100)	275/280 (98.2)	9/17 (52.9)
	H	1/4 (25.0)	16/392 (4.1)	16/23 (69.6)	0/4	7/398 (1.8)	13/22 (59.1)	0/3	3/389 (0.8)	18/30 (60.0)	0/1	4/286 (1.4)	7/13 (53.8)	0/1	3/91 (3.3)	5/8 (62.5)	0/1	3/280 (1.1)	8/17 (47.1)
16	L	1/4 (25.0)	1/379 (0.3)	1/17 (5.9)	2/4 (50.0)	1/401 (0.2)	0/23	3/4 (75.0)	0/376	0/30	0/1	1/274 (0.4)	0/11	1/2 (50.0)	0/89	0/9	0/2	1/272 (0.4)	1/18 (5.6)
	N	2/4	371/379	8/17	2/4	390/401	13/23	1/4	370/376	13/30	1/1	270/274	7/11	1/2	87/89	7/9	2/2	269/272	12/18

		(50·0)	(97·9)	(47·1)	(50·0)	(97·3)	(56·5)	(25·0)	(98·4)	(43·3)	(100)	(98·5)	(63·6)	(50·0)	(97·8)	(77·8)	(100)	(98·9)	(66·7)
	H	1/4 (25·0)	7/379 (1·8)	8/17 (47·1)	0/4	10/401 (2·5)	10/23 (43·5)	0/4	6/376 (1·6)	17/30 (56·7)	0/1	3/274 (1·1)	4/11 (36·4)	0/2	2/89 (2·2)	2/9 (22·2)	0/2	2/272 (0·7)	5/18 (27·8)
52	L	n/a									0/1	2/247 (0·8)	0/11	1/2 (50·0)	0/88	0/9	0/0	2/268 (0·7)	0/17
	N										1/1 (100)	242/247 (98·0)	9/11 (81·8)	1/2 (50·0)	85/88 (96·6)	7/9 (77·8)	0/0	261/268 (97·4)	13/17 (76·5)
	H										0/1	3/247 (1·2)	2/11 (18·2)	0/2	3/88 (3·4)	2/9 (22·2)	0/0	5/268 (1·9)	4/17 (23·5)

H, high; L, low; *n*, total number of patients in the treatment group; *n/N1*, number of patients in category at visit/number of patients in category at baseline; N, normal; n/a, not applicable; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Supplemental Table S4b. Shift from baseline: neutrophils ($\times 10^9/L$)

Study week	Evaluation <i>n/N1</i> (%)	SOLO 1 & 2									CHRONOS								
		Placebo qw (<i>n</i> = 456)			Dupilumab 300 mg q2w (<i>n</i> = 465)			Dupilumab 300 mg qw (<i>n</i> = 455)			Placebo qw + TCS (<i>n</i> = 315)			Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)			Dupilumab 300 mg qw + TCS (<i>n</i> = 315)		
		Baseline status																	
		L	N	H	L	N	H	L	N	H	L	N	H	L	N	H	L	N	H
4	L	3/6 (50·0)	0/398	0/22	1/4 (25·0)	9/418 (2·2)	0/15	1/4 (25·0)	8/404 (2·0)	0/21	0/5	6/273 (2·2)	0/24	0/1	6/90 (6·7)	0/10	3/5 (60·0)	9/268 (3·4)	0/27
	N	3/6 (50·0)	385/398 (96·7)	17/22 (77·3)	3/4 (75·0)	403/418 (96·4)	15/15 (100)	3/4 (75·0)	390/404 (96·5)	17/21 (81·0)	5/5 (100)	254/273 (93·0)	16/24 (66·7)	1/1 (100)	81/90 (90·0)	8/10 (80·0)	2/5 (40·0)	256/268 (95·5)	22/27 (81·5)
	H	0/6	13/398 (3·3)	5/22 (22·7)	0/4	6/418 (1·4)	0/15	0/4	6/404 (1·5)	4/21 (19·0)	0/5	13/273 (4·8)	8/24 (33·3)	0/1	3/90 (3·3)	2/10 (20·0)	0/5	3/268 (1·1)	5/27 (18·5)
16	L	1/6 (16·7)	2/384 (0·5)	0/21	1/4 (25·0)	4/415 (1·0)	0/15	1/4 (25·0)	6/391 (1·5)	0/18	1/5 (20·0)	3/258 (1·2)	0/25	0/1	0/89	0/10	2/6 (33·3)	4/261 (1·5)	0/27
	N	5/6 (83·3)	366/384 (95·3)	17/21 (81·0)	3/4 (75·0)	403/415 (97·1)	15/15 (100)	3/4 (75·0)	376/391 (96·2)	11/18 (61·1)	4/5 (80·0)	245/258 (95·0)	18/25 (72·0)	1/1 (100)	87/89 (97·8)	7/10 (70·0)	4/6 (66·7)	253/261 (96·9)	21/27 (77·8)
	H	0/6	16/384 (4·2)	4/21 (19·0)	0/4	8/415 (1·9)	0/15	0/4	9/391 (2·3)	7/18 (38·9)	0/5	10/258 (3·9)	7/25 (28·0)	0/1	2/89 (2·2)	3/10 (30·0)	0/6	4/261 (1·5)	6/27 (22·2)
52	L	n/a									2/5 (40·0)	0/232	0/23	0/1	3/89 (3·4)	0/10	2/6 (33·3)	7/256 (2·7)	0/25
	N										3/5 (60·0)	225/232 (97·0)	19/23 (82·6)	1/1 (100)	83/89 (93·3)	8/10 (80·0)	4/6 (66·7)	243/256 (94·9)	19/25 (76·0)
	H										0/5	7/232 (3·0)	4/23 (17·4)	0/1	3/89 (3·4)	2/10 (20·0)	0/6	6/256 (2·3)	6/25 (24·0)

H, high; L, low; *n*, total number of patients in the treatment group; N, normal; *n/N1*, number of patients in category at visit/number of patients in category at baseline; n/a, not applicable; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Supplemental Table S4c. Shift from baseline: eosinophils ($\times 10^9/L$)

Study week	Evaluation <i>n/N1</i> (%)	SOLO 1 & 2									CHRONOS									
		Placebo qw (<i>n</i> = 456)			Dupilumab 300 mg q2w (<i>n</i> = 465)			Dupilumab 300 mg qw (<i>n</i> = 455)			Placebo qw + TCS (<i>n</i> = 315)			Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)			Dupilumab 300 mg qw + TCS (<i>n</i> = 315)			
		Baseline status																		
		L	N	H	L	N	H	L	N	H	L	N	H	L	N	H	L	N	H	
4	L	0/0	0/332	0/94	0/0	0/340	0/97	0/0	0/325	0/104	0/0	0/192	0/110	0/0	0/66	0/35	0/0	0/219	0/81	
	N	0/0	302/332 (91·0)	32/94 (34·0)	0/0	297/340 (87·4)	28/97 (28·9)	0/0	282/325 (86·8)	34/104 (32·7)	0/0	177/192 (92·2)	52/110 (47·3)	0/0	60/66 (90·9)	19/35 (54·3)	0/0	198/219 (90·4)	38/81 (46·9)	
	H	0/0	30/332 (9·0)	62/94 (66·0)	0/0	43/340 (12·6)	69/97 (71·1)	0/0	43/325 (13·2)	70/104 (67·3)	0/0	15/192 (7·8)	58/110 (52·7)	0/0	6/66 (9·1)	16/35 (45·7)	0/0	21/219 (9·6)	43/81 (53·1)	
16	L	0/0	0/321	0/90	0/0	0/336	0/98	0/0	0/310	0/103	0/0	0/183	0/105	0/0	0/63	0/37	0/0	0/212	0/82	
	N	0/0	301/321 (93·8)	54/90 (60·0)	0/0	304/336 (90·5)	37/98 (37·8)	0/0	264/310 (85·2)	49/103 (47·6)	0/0	172/183 (94·0)	65/105 (61·9)	0/0	56/63 (88·9)	11/37 (29·7)	0/0	186/212 (87·7)	41/82 (50·0)	
	H	0/0	20/321 (6·2)	36/90 (40·0)	0/0	32/336 (9·5)	61/98 (62·2)	0/0	46/310 (14·8)	54/103 (52·4)	0/0	11/183 (6·0)	40/105 (38·1)	0/0	7/63 (11·1)	26/37 (70·3)	0/0	26/212 (12·3)	41/82 (50·0)	
52	L	n/a										0/0	0/164	0/96	0/0	0/62	0/38	0/0	0/208	0/79
	N											0/0	153/164 (93·3)	67/96 (69·8)	0/0	53/62 (85·5)	26/38 (68·4)	0/0	189/208 (90·9)	54/79 (68·4)
	H											0/0	11/164 (6·7)	29/96 (30·2)	0/0	9/62 (14·5)	12/38 (31·6)	0/0	19/208 (9·1)	25/79 (31·6)

H, high; L, low; n , total number of patients in the treatment group; N, normal; $n/N1$, number of patients in category at visit/number of patients in category at baseline; n/a, not applicable; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Supplemental Table S4d. Shift from baseline: lactate dehydrogenase (IU/L)

Study week	Evaluation <i>n/N1</i> (%)	SOLO 1 & 2									CHRONOS								
		Placebo qw (<i>n</i> = 456)			Dupilumab 300 mg q2w (<i>n</i> = 465)			Dupilumab 300 mg qw (<i>n</i> = 455)			Placebo qw + TCS (<i>n</i> = 315)			Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)			Dupilumab 300 mg qw + TCS (<i>n</i> = 315)		
		Baseline status																	
		L	N	H	L	N	H	L	N	H	L	N	H	L	N	H	L	N	H
4	L	3/6 (50·0)	5/314 (1·6)	0/114	3/6 (50·0)	13/328 (4·0)	0/112	4/7 (57·1)	14/312 (4·5)	1/118 (0·8)	0/0	0/147	0/145	0/0	0/41	0/53	0/0	0/143	0/147
	N	3/6 (50·0)	277/314 (88·2)	43/114 (37·7)	3/6 (50·0)	310/328 (94·5)	89/112 (79·5)	3/7 (42·9)	292/312 (93·6)	91/118 (77·1)	0/0	133/147 (90·5)	49/145 (33·8)	0/0	41/41 (100)	41/53 (77·4)	0/0	139/143 (97·2)	115/147 (78·2)
	H	0/6	32/314 (10·2)	71/114 (62·3)	0/6	5/328 (1·5)	23/112 (20·5)	0/7	6/312 (1·9)	26/118 (22·0)	0/0	14/147 (9·5)	96/145 (66·2)	0/0	0/41	12/53 (22·6)	0/0	4/143 (2·8)	32/147 (21·8)
16	L	3/6 (50·0)	8/304 (2·6)	0/109	2/6 (33·3)	14/322 (4·3)	0/114	6/6 (100)	24/299 (8·0)	0/117	0/0	0/126	0/143	0/0	0/39	0/56	0/0	0/133	0/143
	N	3/6 (50·0)	276/304 (90·8)	56/109 (51·4)	4/6 (66·7)	305/322 (94·7)	104/114 (91·2)	0/6	275/299 (92·0)	108/117 (92·3)	0/0	111/126 (88·1)	59/143 (41·3)	0/0	39/39 (100)	45/56 (80·4)	0/0	132/133 (99·2)	129/143 (90·2)
	H	0/6	20/304 (6·6)	53/109 (48·6)	0/6	3/322 (0·9)	10/114 (8·8)	0/6	0/299	9/117 (7·7)	0/0	15/126 (11·9)	84/143 (58·7)	0/0	0/39	11/56 (19·6)	0/0	1/133 (0·8)	14/143 (9·8)
52	L	n/a									0/0	0/119	0/124	0/0	0/42	0/52	0/0	0/131	0/140
	N										0/0	115/119 (96·6)	65/124 (52·4)	0/0	41/42 (97·6)	48/52 (92·3)	0/0	129/131 (98·5)	132/140 (94·3)
	H										0/0	4/119 (3·4)	59/124 (47·6)	0/0	1/42 (2·4)	4/52 (7·7)	0/0	2/131 (1·5)	8/140 (5·7)

Normal range: 135–330 U/L (female) and 135–281 U/L (male) in SOLO 1 & 2, respectively and 53–234 U/L in CHRONOS. H, high; L, low; *n*, total number of patients in the treatment group; N, normal; *n/N1*, number of patients in category at visit/number of patients in category at baseline; n/a, not applicable; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Supplemental Table S5. Adverse events (based on MedDRA-Preferred Term) in dupilumab-treated patients^a with an eosinophil count > $5.0 \times 10^9/L$ at any visit in SOLO 1 & 2 and CHRONOS

Patients with AE, <i>n</i> (%)	SOLO 1 & 2		CHRONOS	
	Dupilumab 300 mg q2w (<i>n</i> = 5)	Dupilumab 300 mg qw (<i>n</i> = 3)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 2)	Dupilumab 300 mg qw + TCS (<i>n</i> = 2)
Allergic keratitis	0	0	1 (50.0)	0
Androgenetic alopecia	1 (20.0)	0	0	0
Arthralgia	1 (20.0)	0	0	0
Blepharitis	0	0	2 (100)	0
Blood cholesterol increased	0	0	1 (50.0)	0
Blood lactate dehydrogenase increased	0	0	1 (50.0)	0
Blood uric acid increased	0	0	1 (50.0)	0
Bone pain	0	0	1 (50.0)	0
Cellulitis	0	1 (33.3)	0	0
Cerebral infarction	0	0	1 (50.0) ^b	0
Chest pain	0	0	1 (50.0)	0
Chills	0	0	1 (50.0)	0
Conjunctivitis	1 (20.0)	0	0	0
Conjunctivitis allergic	0	0	1 (50.0)	1 (50.0)
Depression	0	0	1 (50.0)	0
Dermatitis atopic	1 (20.0)	2 (66.7)	2 (100)	1 (50.0)
Dermatitis exfoliative	0	0	1 (50.0)	0
Eosinophil count increased	1 (20.0)	0	1 (50.0)	0

	SOLO 1 & 2		CHRONOS	
Patients with AE, <i>n</i> (%)	Dupilumab 300 mg q2w (<i>n</i> = 5)	Dupilumab 300 mg qw (<i>n</i> = 3)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 2)	Dupilumab 300 mg qw + TCS (<i>n</i> = 2)
Eosinophilia	1 (20·0)	0	0	0
Epistaxis	0	1 (33·3)	0	0
Eye pruritus	0	1 (33·3)	0	0
Fall	0	1 (33·3)	0	0
Gout	0	0	1 (50·0)	0
Hyperhidrosis	0	0	1 (50·0)	1 (50·0)
Impetigo	0	1 (33·3)	0	0
Injection site reaction	1 (20·0)	0	0	0
Insomnia	0	0	0	1 (50·0)
Labyrinthitis	0	0	0	1 (50·0)
Migraine	0	0	0	1 (50·0)
Musculoskeletal pain	0	0	0	1 (50·0)
Nasopharyngitis	0	1 (33·3)	0	1 (50·0)
Ocular hyperaemia	0	1 (33·3)	1 (50·0)	0
Photophobia	0	0	0	1 (50·0)
Psychotic disorder	0	0	1 (50·0)	0
Seasonal allergy	0	0	1 (50·0)	0
Sinusitis	0	0	0	2 (100)
Superinfection bacterial	0	0	1 (50·0)	0
Tinea pedis	0	0	0	1 (50·0)
Upper respiratory tract infection	0	0	0	1 (50·0)

	SOLO 1 & 2		CHRONOS	
Patients with AE, <i>n</i> (%)	Dupilumab 300 mg q2w (<i>n</i> = 5)	Dupilumab 300 mg qw (<i>n</i> = 3)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 2)	Dupilumab 300 mg qw + TCS (<i>n</i> = 2)
Urinary tract infection	0	0	0	1 (50·0)
Viral upper respiratory tract infection	0	0	0	1 (50·0)
Weight increased	0	0	1 (50·0)	0

^aNo adverse events were reported for patients in the placebo group who had an eosinophil count $> 5·0 \times 10^9/L$ at any visit in SOLO 1 & 2 and CHRONOS. ^bA 47-year-old male with history of hypertension, prior ischaemic stroke and eosinophilia was randomised to dupilumab 300 mg q2w + TCS and treated for 5 weeks before dropping out because of erythroderma. He suffered cerebral infarction 21 days after stopping dupilumab. This was considered not to be related to the study drug. AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids.

Supplemental Table S6a. Summary statistics for haematology laboratory parameters in patients who discontinued study treatment due to [haematological TEAEs](#) or [any TEAE](#): red blood cells and platelets. Values that are noticeably higher or lower than the overall population are highlighted in yellow.

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Haematocrit (ratio)	NR	Female: 0.3–0.5 Male: 0.4–0.5			Female: 0.3–0.5 Male: 0.4–0.5		
	BL	0	0.4 (0.4, 0.4), 1	0.5 (0.5, 0.5), 1	0.5 (0.5, 0.5), 1	0	0
		0.4 (0.4, 0.4), 7	0.4 (0.4, 0.5), 6	0.5 (0.4, 0.5), 7	0.4 (0.4, 0.5), 26	0.4 (0.4, 0.5), 3	0.4 (0.4, 0.4), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	4	0	0.4 (0.4, 0.4), 1	0.5 (0.5, 0.5), 1	0.5 (0.5, 0.5), 1	0	0
		0.5 (0.4, 0.5), 3	0.4 (0.4, 0.5), 4	0.4 (0.4, 0.5), 5	0.4 (0.4, 0.5), 25	0.4 (0.4, 0.5), 2	0.4 (0.4, 0.5), 9
	16	0	0.5 (0.5, 0.5), 1	0.5 (0.5, 0.5), 1	0	0	0
		0.4 (0.4, 0.4), 1	0.5 (0.4, 0.5), 3	0.5 (0.4, 0.5), 3	0.4 (0.4, 0.5), 21	0.4 (0.4, 0.5), 2	0.4 (0.4, 0.4), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	0.4 (0.4, 0.5), 14	0.5 (0.5, 0.5), 1	0.5 (0.4, 0.5), 3

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Haemoglobin (g/L)	NR	Female: 110·0–155·0 Male: 125·0–170·0			Female: 115·0–164·0 Male: 125·0–181·0		
	BL	0	132·0 (132·0, 132·0), 1	149·0 (149·0, 149·0), 1	163·0 (163·0, 163·0), 1	0	0
		138·0 (117·0, 149·0), 7	133·5 (130·0, 152·0), 6	147·0 (124·0, 149·0), 7	142·0 (125·0, 153·0), 26	143·0 (121·0, 149·0), 3	139·0 (134·0, 160·0), 9
	4	0	136·0 (136·0, 136·0), 1	143·0 (143·0, 143·0), 1	150·0 (150·0, 150·0), 1	0	0
		145·0 (117·0, 152·0), 3	140·5 (133·5, 151·0), 4	131·0 (127·0, 143·0), 5	140·0 (127·0, 150·0), 25	146·0 (125·0, 167·0), 2	145·0 (133·0, 151·0), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	16	0	155·0 (155·0, 155·0), 1	152·0 (152·0, 152·0), 1	0	0	0
		131·0 (131·0, 131·0), 1	155·0 (138·0, 156·0), 3	147·0 (112·0, 152·0), 3	144·0 (133·0, 153·0), 21	137·0 (122·0, 151·0), 2	140·0 (130·0, 151·0), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	149·0 (137·0, 152·0), 14	156·0 (156·0, 156·0), 1	154·0 (145·0, 167·0), 3
Erythrocyte mean Corpuscular haemoglobin	NR	27·0–34·0			26·0–34·0		
	BL	0	31·0 (31·0, 31·0), 1	31·7 (31·7, 31·7), 1	29·0 (29·0, 29·0), 1	0	0

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
(pg)		30.5 (26.2, 30.8), 7	30.9 (30.5, 32.1), 6	29.9 (28.7, 31.7), 7	31.0 (29.0, 31.0), 26	30.0 (28.0, 32.0), 3	31.0 (29.0, 32.0), 9
	4	0	31.0 (31.0, 31.0), 1	31.7 (31.7, 31.7), 1	29.0 (29.0, 29.0), 1	0	0
		30.8 (27.8, 30.9), 3	30.9 (30.3, 31.3), 4	30.6 (28.0, 31.7), 5	30.0 (29.0, 31.0), 25	30.0 (27.0, 33.0), 2	31.0 (30.0, 31.0), 9
	16	0	29.6 (29.6, 29.6), 1	32.2 (32.2, 32.2), 1	0	0	0
		28.6 (28.6, 28.6), 1	29.6 (29.0, 29.9), 3	29.6 (25.0, 32.2), 3	30.0 (29.0, 32.0), 21	29.0 (27.0, 31.0), 2	29.5 (28.5, 32.5), 4
	52	n/a	n/a	n/a	0	0	0

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	31·0 (30·0, 32·0), 14	31·0 (31·0, 31·0), 1	30·0 (29·0, 34·0), 3
Erythrocyte mean corpuscular haemoglobin concentration (g/L)	NR	310·0–360·0			310·0–380·0		
	BL	0	329·0 (329·0, 329·0), 1	316·0 (316·0, 316·0), 1	344·0 (344·0, 344·0), 1	0	0
		319·0 (308·0, 322·0), 7	330·5 (326·0, 332·0), 6	320·0 (316·0, 324·0), 7	330·0 (327·0, 340·0), 26	332·0 (326·0, 337·0), 3	342·0 (340·0, 350·0), 9
	4	0	332·0 (332·0, 332·0), 1	316·0 (316·0, 316·0), 1	332·0 (332·0, 332·0), 1	0	0
		319·0 (313·0, 327·0), 3	332·5 (330·5, 336·5), 4	320·0 (316·0, 320·0), 5	334·0 (330·0, 340·0), 25	333·0 (332·0, 334·0), 2	340·0 (334·0, 341·0), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	16	0	318·0 (318·0, 318·0), 1	323·0 (323·0, 323·0), 1	0	0	0
		328·0 (328·0, 328·0), 1	318·0 (306·0, 318·0), 3	323·0 (306·0, 324·0), 3	336·0 (321·0, 341·0), 21	332·0 (332·0, 332·0), 2	340·0 (337·0, 349·5), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	340·0 (325·0, 350·0), 14	344·0 (344·0, 344·0), 1	340·0 (337·0, 344·0), 3
Erythrocyte mean corpuscular	NR	Female: 82·0–102·0 Male: 78·0–100·0			79·0–100·0		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
volume (fL)	BL	0	94.2 (94.2, 94.2), 1	100.2 (100.2, 100.2), 1	84.0 (84.0, 84.0), 1	0	0
		91.7 (88.1, 96.1), 7	93.2 (91.8, 96.5), 6	93.4 (89.1, 100.2), 7	90.0 (86.0, 93.0), 26	90.0 (82.0, 97.0), 3	91.0 (86.0, 92.0), 9
	4	0	93.5 (93.5, 93.5), 1	100.4 (100.4, 100.4), 1	86.0 (86.0, 86.0), 1	0	0
		94.4 (87.1, 98.4), 3	93.0 (90.0, 94.7), 4	93.5 (87.6, 100.4), 5	89.0 (85.0, 94.0), 25	89.0 (80.0, 98.0), 2	91.0 (85.0, 95.0), 9
	16	0	93.1 (93.1, 93.1), 1	99.5 (99.5, 99.5), 1	0	0	0
		87.2 (87.2, 93.1), 1	93.1 (91.0, 94.7), 4	91.4 (81.5, 100.4), 5	92.0 (86.0, 97.0), 3	87.5 (82.0, 97.0), 3	85.5 (83.5, 92.0), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs <i>or any TEAE</i>		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		87·2), 1	97·7), 3	99·5), 3	95·0), 21	93·0), 2	94·5), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	92·0 (87·0, 93·0), 14	90·0 (90·0, 90·0), 1	90·0 (86·0, 100·0), 3
Platelets (x 10⁹/L)	NR	125·0–375·0			130·0–400·0		
	BL	0	456·0 (456·0, 456·0), 1	217·0 (217·0, 217·0), 1	193·0 (193·0, 193·0), 1	0	0
		342·0 (234·0, 397·0), 7	249·0 (237·0, 304·0), 6	278·0 (217·0, 330·0), 7	278·5 (230·0, 323·0), 26	256·0 (249·0, 422·0), 3	223·0 (190·0, 284·0), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	4	0	382·0 (382·0, 382·0), 1	211·0 (211·0, 211·0), 1	201·0 (201·0, 201·0), 1	0	0
		215·0 (171·0, 371·0), 3	266·0 (255·0, 326·0), 4	245·0 (225·0, 280·0), 5	264·5 (224·5, 309·0), 24	329·0 (240·0, 418·0), 2	219·0 (190·0, 291·0), 9
	16	0	368·0 (368·0, 368·0), 1	198·0 (198·0, 198·0), 1	0	0	0
		260·0 (260·0, 260·0), 1	273·0 (201·0, 368·0), 3	277·0 (198·0, 313·0), 3	262·0 (237·0, 295·0), 21	269·5 (253·0, 286·0), 2	270·5 (189·5, 326·5), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	296·0 (245·0, 317·0), 14	290·0 (290·0, 290·0), 1	291·0 (205·0, 361·0), 3

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Erythrocytes (x 10¹²/L)	NR	Female: 3·7–5·2 Male: 4·0–5·6			Female: 3·9–5·6 Male: 4·0–6·4		
	BL	0	4·3 (4·3, 4·3), 1	4·7 (4·7, 4·7), 1	5·6 (5·6, 5·6), 1	0	0
		4·5 (4·3, 4·8), 7	4·4 (4·2, 4·7), 6	4·7 (4·3, 4·9), 7	4·8 (4·3, 5·1), 26	4·7 (4·4, 4·8), 3	4·9 (4·4, 5·1), 9
	4	0	4·4 (4·4, 4·4), 1	4·5 (4·5, 4·5), 1	5·2 (5·2, 5·2), 1	0	0
		4·7 (4·2, 4·9), 3	4·6 (4·3, 5·0), 4	4·5 (4·3, 4·7), 5	4·7 (4·5, 4·9), 25	4·9 (4·7, 5·1), 2	4·9 (4·3, 5·1), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n1</i> For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	16	0	5.2 (5.2, 5.2), 1	4.7 (4.7, 4.7), 1	0	0	0
		4.6 (4.6, 4.6), 1	5.2 (4.8, 5.2), 3	4.7 (4.5, 5.0), 3	4.7 (4.4, 5.0), 21	4.7 (4.5, 4.9), 2	4.8 (4.2, 5.2), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	4.8 (4.5, 5.1), 14	5.0 (5.0, 5.0), 1	5.2 (4.2, 5.5), 3

BL, baseline; *n*, total number of patients in the treatment group; *n1*, number of patients at visit; n/a, not applicable; NR, normal range; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids; TEAE, treatment-emergent adverse event.

Supplemental Table S6b. Summary statistics for haematology laboratory parameters in patients who discontinued study treatment due to [haematological TEAEs](#) or [any TEAE](#): white blood cells. Values that are noticeably higher or lower than the overall population are highlighted in yellow.

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Basophils (x 10 ⁹ /L)	NR	0.0–0.3			0.0–0.2		
	BL	0	0.1 (0.1, 0.1), 1	0.0 (0.0, 0.0), 1	0.1 (0.1, 0.1), 1	0	0
		0.0 (0.0, 0.0), 7	0.0 (0.0, 0.0), 6	0.0 (0.0, 0.0), 7	0.0 (0.0, 0.1), 26	0.1 (0.0, 0.1), 3	0.0 (0.0, 0.0), 9
	4	0	0.0 (0.0, 0.0), 1	0.0 (0.0, 0.0), 1	0.0 (0.0, 0.0), 1	0	0

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		0.0 (0.0, 0.0), 3	0.0 (0.0, 0.0), 4	0.0 (0.0, 0.0), 5	0.1 (0.0, 0.1), 25	0.0 (0.0, 0.0), 2	0.0 (0.0, 0.1), 9
	16	0	0.0 (0.0, 0.0), 1	0.0 (0.0, 0.0), 1	0	0	0
		0.0 (0.0, 0.0), 1	0.0 (0.0, 0.0), 3	0.0 (0.0, 0.0), 3	0.0 (0.0, 0.0), 21	0.1 (0.1, 0.1), 2	0.0 (0.0, 0.0), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	0.0 (0.0, 0.1), 14	0.1 (0.1, 0.1), 1	0.0 (0.0, 0.0), 3
Basophils/	NR	0.0–3.0			0.0–2.0		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
leukocytes (%)	BL	0	0.7 (0.7, 0.7), 1	0.4 (0.4, 0.4), 1	1.0 (1.0, 1.0), 1	0	0
		0.4 (0.2, 0.5), 7	0.4 (0.2, 0.5), 6	0.2 (0.2, 0.4), 7	0.6 (0.3, 1.0), 26	0.4 (0.3, 0.5), 3	0.6 (0.5, 0.7), 9
	4	0	0.2 (0.2, 0.2), 1	0.3 (0.3, 0.3), 1	1.3 (1.3, 1.3), 1	0	0
		0.1 (0.1, 0.2), 3	0.3 (0.2, 0.4), 4	0.3 (0.3, 0.3), 5	0.6 (0.4, 1.2), 25	0.2 (0.0, 0.3), 2	0.7 (0.6, 0.8), 9
	16	0	0.4 (0.4, 0.4), 1	0.3 (0.3, 0.3), 1	0	0	0
		0.2	0.4	0.3	0.6	0.8	0.7

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		(0·2, 0·2), 1	(0·0, 0·7), 3	(0·1, 0·6), 3	(0·4, 0·6), 21	(0·7, 0·9), 2	(0·6, 0·8), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	0·5 (0·3, 1·3), 14	0·7 (0·7, 0·7), 1	0·5 (0·4, 0·5), 3
Eosinophils (x 10 ⁹ /L)	NR	0·0–0·8			0·0–0·6		
	BL	0	2·4 (2·4, 2·4), 1	0·4 (0·4, 0·4), 1	0·2 (0·2, 0·2), 1	0	0
		0·4 (0·3, 0·6), 7	1·1 (0·4, 2·4), 6	0·4 (0·3, 1·1), 7	0·5 (0·2, 0·9), 26	0·5 (0·4, 3·2), 3	0·4

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
							(0.2, 0.5), 9
	4	0	1.2 (1.2, 1.2), 1	0.3 (0.3, 0.3), 1	0.2 (0.2, 0.2), 1	0	0
		0.3 (0.0, 0.9), 3	0.7 (0.1, 1.5), 4	0.6 (0.6, 1.2), 5	0.3 (0.2, 0.7), 25	5.7 (0.4, 11.1), 2	0.4 (0.2, 0.5), 9
	16	0	2.3 (2.3, 2.3), 1	0.2 (0.2, 0.2), 1	0	0	0
		0.9 (0.9, 0.9), 1	1.0 (0.0, 2.3), 3	0.9 (0.2, 2.3), 3	0.2 (0.1, 0.5), 21	2.3 (0.4, 4.1), 2	0.4 (0.3, 0.7), 4

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	0.4 (0.1, 0.5), 14	2.6 (2.6, 2.6), 1	0.2 (0.2, 0.4), 3
Eosinophils/ leukocytes (%)	NR	0.0–7.0			0.0–6.8		
	BL	0	26.0 (26.0, 26.0), 1	3.4 (3.4, 3.4), 1	4.0 (4.0, 4.0), 1	0	0
		5.6 (4.2, 9.3), 7	12.5 (7.2, 26.0), 6	5.6 (3.9, 15.4), 7	7.1 (3.2, 11.7), 26	5.2 (2.7, 23.5), 3	5.1 (3.6, 7.5), 9
	4	0	15.6 (15.6, 15.6), 1	2.5 (2.5, 2.5), 1	4.4 (4.4, 4.4), 1	0	0

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	16	3.8 (1.2, 8.6), 3	8.2 (0.4, 20.6), 4	10.7 (9.0, 17.4), 5	5.3 (3.4, 9.3), 25	23.8 (5.6, 42.0), 2	6.3 (3.7, 7.1), 9
		0	33.0 (33.0, 33.0), 1	1.4 (1.4, 1.4), 1	0	0	0
		14.2 (14.2, 14.2), 1	11.9 (0.0, 33.0), 3	12.8 (1.4, 27.1), 3	3.9 (2.0, 5.8), 21	16.6 (5.6, 27.6), 2	7.9 (5.2, 10.2), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	4.5 (2.4, 6.9), 14	19.4 (19.4, 19.4), 1	2.9 (2.4, 5.8), 3
Lymphocytes	NR	0.9–3.6			0.8–4.3		

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
(x 10 ⁹ /L)	BL	0	3·0 (3·0, 3·0), 1	6·2 (6·2, 6·2), 1	1·6 (1·6, 1·6), 1	0	0
		1·3 (1·2, 2·1), 7	1·6 (1·6, 2·3), 6	1·4 (0·8, 2·5), 7	1·4 (1·2, 1·7), 26	1·6 (1·4, 2·6), 3	1·5 (1·5, 1·9), 9
	4	0	3·9 (3·9, 3·9), 1	6·9 (6·9, 6·9), 1	1·2 (1·2, 1·2), 1	0	0
		2·4 (1·2, 2·7), 3	2·7 (1·7, 3·8), 4	2·0 (1·5, 2·4), 5	1·5 (1·2, 1·7), 25	2·1 (1·8, 2·4), 2	1·8 (1·5, 1·9), 9
	16	0	3·0 (3·0, 3·0), 1	7·0 (7·0, 7·0), 1	0	0	0
		1·6	2·2	2·0	1·4	1·9	1·7

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), n1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (n = 456)	Dupilumab 300 mg q2w (n = 465)	Dupilumab 300 mg qw (n = 455)	Placebo qw + TCS (n = 315)	Dupilumab 300 mg q2w + TCS (n = 110)	Dupilumab 300 mg qw + TCS (n = 315)
		(1·6, 1·6), 1	(0·4, 3·0), 3	(1·5, 7·0), 3	(1·2, 1·9), 21	(1·3, 2·5), 2	(1·5, 2·0), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	1·5 (1·2, 1·7), 14	2·6 (2·6, 2·6), 1	1·9 (1·6, 1·9), 3
Lymphocytes/ leukocytes (%)	NR	12·0–46·0			15·4–48·5		
	BL	0	32·0 (32·0, 32·0), 1	50·0 (50·0, 50·0), 1	33·3 (33·3, 33·3), 1	0	0
		23·3 (22·6, 28·3), 7	26·8 (19·6, 30·7), 6	18·2 (13·1, 25·0), 7	20·4 (16·4, 28·6), 26	15·5 (12·2, 19·8), 3	24·6 (23·1, 27·4), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	4	0	49.2 (49.2, 49.2), 1	58.0 (58.0, 58.0), 1	35.8 (35.8, 35.8), 1	0	0
		28.2 (22.2, 35.6), 3	29.8 (22.6, 42.8), 4	29.3 (21.4, 29.5), 5	22.8 (17.8, 27.0), 25	17.0 (9.0, 24.9), 2	26.4 (24.5, 29.4), 9
	16	0	42.2 (42.2, 42.2), 1	55.6 (55.6, 55.6), 1	0	0	0
		24.8 (24.8, 24.8), 1	26.4 (6.6, 42.2), 3	29.0 (17.6, 55.6), 3	21.7 (18.0, 31.0), 21	17.6 (16.6, 18.5), 2	28.8 (25.8, 31.5), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	21.2 (17.3, 22.8), 14	19.5 (19.5, 19.5), 1	28.4 (17.3, 29.7), 3

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Monocytes (x 10 ⁹ /L)	NR	0.0–1.2			0.1–0.9		
	BL	0	0.2 (0.2, 0.2), 1	0.5 (0.5, 0.5), 1	0.2 (0.2, 0.2), 1	0	0
		0.5 (0.4, 0.6), 7	0.5 (0.2, 0.6), 6	0.5 (0.3, 0.6), 7	0.4 (0.3, 0.5), 26	0.5 (0.3, 0.7), 3	0.4 (0.4, 0.4), 9
	4	0	0.3 (0.3, 0.3), 1	0.4 (0.4, 0.4), 1	0.2 (0.2, 0.2), 1	0	0
		0.4 (0.3, 0.6), 3	0.4 (0.3, 0.8), 4	0.4 (0.4, 0.5), 5	0.4 (0.3, 0.5), 25	0.9 (0.3, 1.6), 2	0.4 (0.3, 0.4), 9
	16	0	0.2 (0.2, 0.2), 1	0.5 (0.5, 0.5), 1	0	0	0

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		0.5 (0.5, 0.5), 1	0.2 (0.0, 0.7), 3	0.5 (0.4, 0.5), 3	0.4 (0.3, 0.5), 21	0.4 (0.4, 0.5), 2	0.3 (0.3, 0.4), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	0.4 (0.3, 0.5), 14	0.7 (0.7, 0.7), 1	0.5 (0.4, 0.6), 3
Monocytes/ leukocytes (%)	NR	0.0–11.0			2.6–10.1		
	BL	0	2.3 (2.3, 2.3), 1	3.9 (3.9, 3.9), 1	4.7 (4.7, 4.7), 1	0	0
		8.0 (4.9, 9.3), 7	5.7 (2.9, 7.1), 6	4.8 (3.9, 6.9), 7	5.4 (4.9, 6.2), 26	4.0 (3.7, 4.2), 3	6.3 (5.4, 7.0), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	4	0	3·9 (3·9, 3·9), 1	3·8 (3·8, 3·8), 1	6·8 (6·8, 6·8), 1	0	0
		7·1 (3·6, 7·8), 3	5·7 (4·7, 6·3), 4	6·6 (4·2, 7·6), 5	6·1 (5·0, 6·9), 25	4·9 (3·7, 6·0), 2	6·1 (5·7, 7·2), 9
	16	0	2·2 (2·2, 2·2), 1	3·8 (3·8, 3·8), 1	0	0	0
		8·3 (8·3, 8·3), 1	2·2 (0·5, 9·0), 3	4·1 (3·8, 7·8), 3	6·0 (4·8, 7·1), 21	4·4 (3·3, 5·5), 2	6·0 (5·5, 6·4), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	5·7 (5·0, 6·0), 14	5·1 (5·1, 5·1), 1	6·1 (4·9, 8·6), 3

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Neutrophils (x 10 ⁹ /L)	NR	1.7–7.9			2.0–7.2		
	BL	0	3.6 (3.6, 3.6), 1	5.2 (5.2, 5.2), 1	2.8 (2.8, 2.8), 1	0	0
		3.3 (2.9, 4.6), 7	3.7 (3.6, 4.5), 6	5.0 (4.6, 5.5), 7	4.0 (3.3, 5.5), 26	8.1 (5.0, 12.9), 3	3.9 (3.2, 4.2), 9
	4	0	2.5 (2.5, 2.5), 1	4.2 (4.2, 4.2), 1	1.7 (1.7, 1.7), 1	0	0
		4.0 (2.7, 7.1), 3	3.0 (2.6, 7.5), 4	3.5 (3.4, 3.8), 5	4.2 (3.6, 4.9), 25	8.1 (4.8, 11.3), 2	3.7 (3.3, 3.9), 9
	16	0	1.6 (1.6, 1.6), 1	4.9 (4.9, 4.9), 1	0	0	0

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), n1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (n = 456)	Dupilumab 300 mg q2w (n = 465)	Dupilumab 300 mg qw (n = 455)	Placebo qw + TCS (n = 315)	Dupilumab 300 mg q2w + TCS (n = 110)	Dupilumab 300 mg qw + TCS (n = 315)
		3.3 (3.3, 3.3), 1	4.2 (1.6, 5.9), 3	4.3 (3.4, 4.9), 3	4.5 (3.1, 5.9), 21	6.3 (4.9, 7.7), 2	3.4 (3.1, 3.8), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	4.9 (4.5, 6.0), 14	7.3 (7.3, 7.3), 1	3.8 (3.8, 6.9), 3
Neutrophils/ leukocytes (%)	NR	46.0–72.0			40.5–75.0		
	BL	0	39.0 (39.0, 39.0), 1	42.3 (42.3, 42.3), 1	57.0 (57.0, 57.0), 1	0	0
		57.7 (57.0, 62.7), 7	55.8 (39.0, 67.2), 6	63.4 (49.4, 74.9), 7	64.6 (55.8, 68.6), 26	70.4 (60.1, 77.4), 3	63.3 (60.4, 64.8), 9

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
	4	0	31.1 (31.1, 31.1), 1	35.4 (35.4, 35.4), 1	52.0 (52.0, 52.0), 1	0	0
		63.4 (52.6, 65.5), 3	51.5 (38.3, 64.0), 4	51.3 (41.5, 53.3), 5	64.0 (57.7, 68.4), 25	54.3 (43.0, 65.6), 2	62.0 (59.6, 63.1), 9
	16	0	22.2 (22.2, 22.2), 1	38.9 (38.9, 38.9), 1	0	0	0
		52.5 (52.5, 52.5), 1	52.0 (22.2, 92.9), 3	49.8 (38.9, 51.1), 3	63.8 (57.9, 73.0), 21	60.6 (51.6, 69.6), 2	55.7 (51.5, 62.7), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	67.1 (62.8, 73.1), 14	55.3 (55.3, 55.3), 1	60.8 (56.6, 75.0), 3

Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n</i> 1 For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
Leukocytes (x 10 ⁹ /L)	NR	3.7–11.0			3.8–10.7		
	BL	0	9.4 (9.4, 9.4), 1	12.4 (12.4, 12.4), 1	4.9 (4.9, 4.9), 1	0	0
		6.5 (5.3, 8.1), 7	8.8 (5.5, 9.6), 6	7.4 (7.2, 10.1), 7	6.1 (5.6, 8.5), 26	13.5 (7.2, 16.7), 3	6.0 (5.4, 6.7), 9
	4	0	8.0 (8.0, 8.0), 1	11.9 (11.9, 11.9), 1	3.3 (3.3, 3.3), 1	0	0
		7.7 (4.3, 10.9), 3	7.6 (6.0, 12.3), 4	7.1 (6.7, 8.3), 5	6.7 (5.6, 7.1), 25	16.8 (7.3, 26.4), 2	6.0 (6.0, 6.4), 9
	16	0	7.0 (7.0, 7.0), 1	12.7 (12.7, 12.7), 1	0	0	0

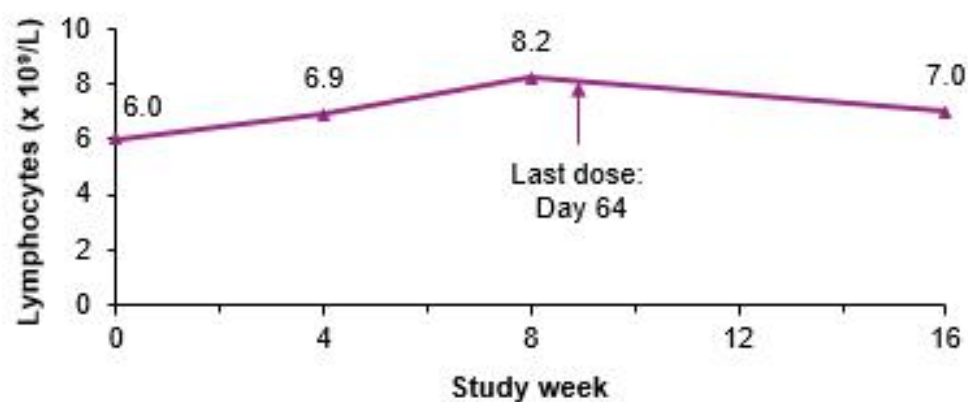
Laboratory parameter	Study week	SOLO 1 & 2			CHRONOS		
Median (Q1, Q3), <i>n1</i> For patients who discontinued due to: haematological TEAEs or any TEAE		Placebo qw (<i>n</i> = 456)	Dupilumab 300 mg q2w (<i>n</i> = 465)	Dupilumab 300 mg qw (<i>n</i> = 455)	Placebo qw + TCS (<i>n</i> = 315)	Dupilumab 300 mg q2w + TCS (<i>n</i> = 110)	Dupilumab 300 mg qw + TCS (<i>n</i> = 315)
		6.3 (6.3, 6.3), 1	7.0 (6.3, 8.1), 3	8.4 (6.8, 12.7), 3	6.6 (5.7, 8.1), 21	11.0 (7.1, 14.9), 2	6.0 (5.5, 6.6), 4
	52	n/a	n/a	n/a	0	0	0
		n/a	n/a	n/a	7.4 (6.0, 8.6), 14	13.1 (13.1, 13.1), 1	6.7 (6.3, 9.2), 3

BL, baseline; *n*, total number of patients in the treatment group; *n1*, number of patients at visit; n/a, not applicable; NR, normal range; Q1, quartile 1; Q3, quartile 3; qw, once weekly; q2w, every 2 weeks; TCS, topical corticosteroids; TEAE, treatment-emergent adverse event.

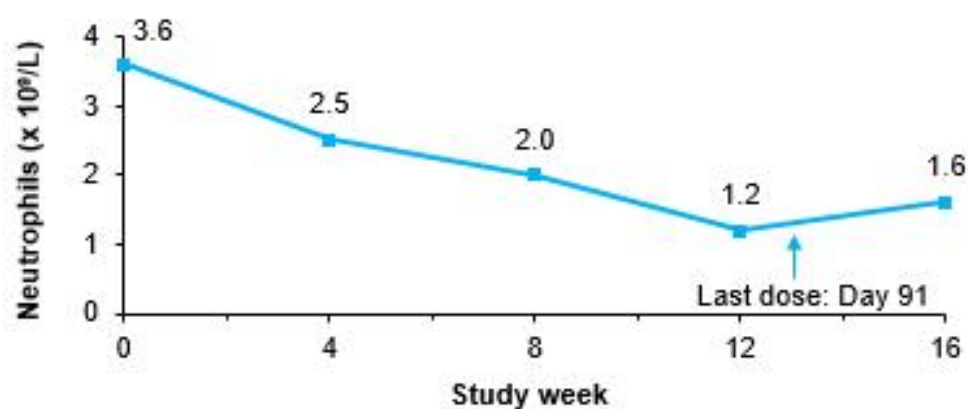
Supplemental Fig. S1. Haematological data over time in patients who withdrew due to haematological adverse events.

(a) Absolute lymphocyte counts in the patient in SOLO 1 (dupilumab 300 mg qw) who withdrew due to lymphocytosis. (b) Absolute neutrophil counts in the patient in SOLO 2 (dupilumab 300 mg q2w) who withdrew due to neutropenia. (c) Absolute neutrophil counts in the patient in CHRONOS (placebo + TCS) who withdrew due to neutropenia. Normal ranges: lymphocytes, $0.9\text{--}3.6 \times 10^9/\text{L}$ (SOLO), $0.8\text{--}4.3 \times 10^9/\text{L}$ (CHRONOS); neutrophils, $1.7\text{--}7.9 \times 10^9/\text{L}$ (SOLO), $2.0\text{--}7.2 \times 10^9/\text{L}$ (CHRONOS).

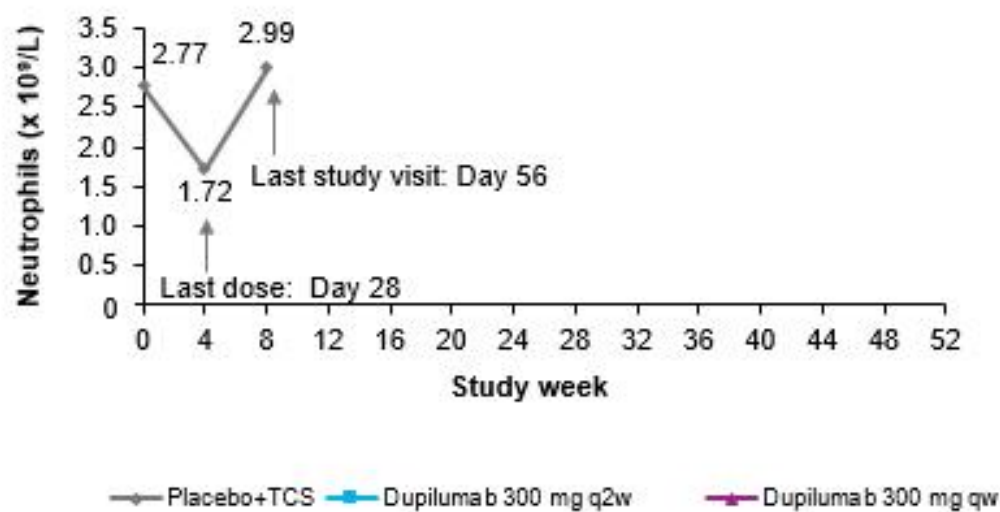
(a)



(b)



(c)



Reference

1. US Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research. Toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials. Available at: <https://www.fda.gov/downloads/BiologicsBloodVaccines/ucm091977> (last accessed 10 December 2018).