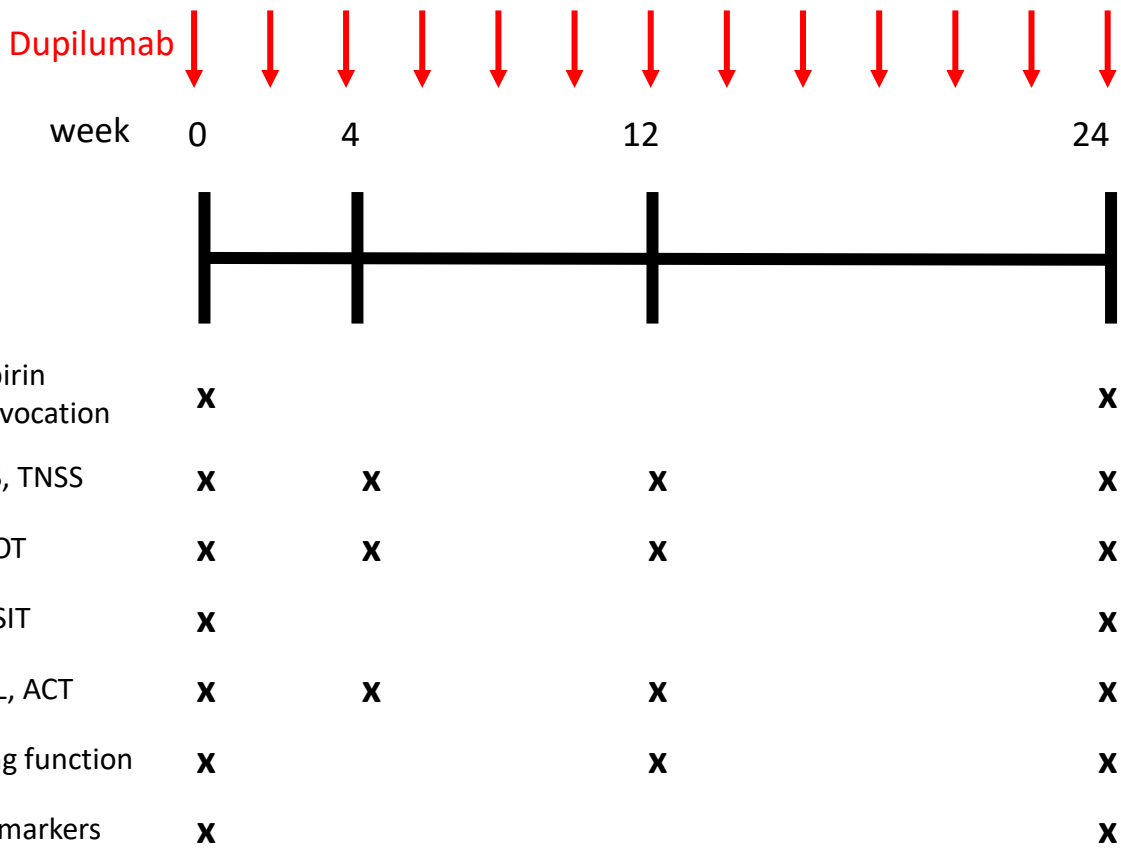
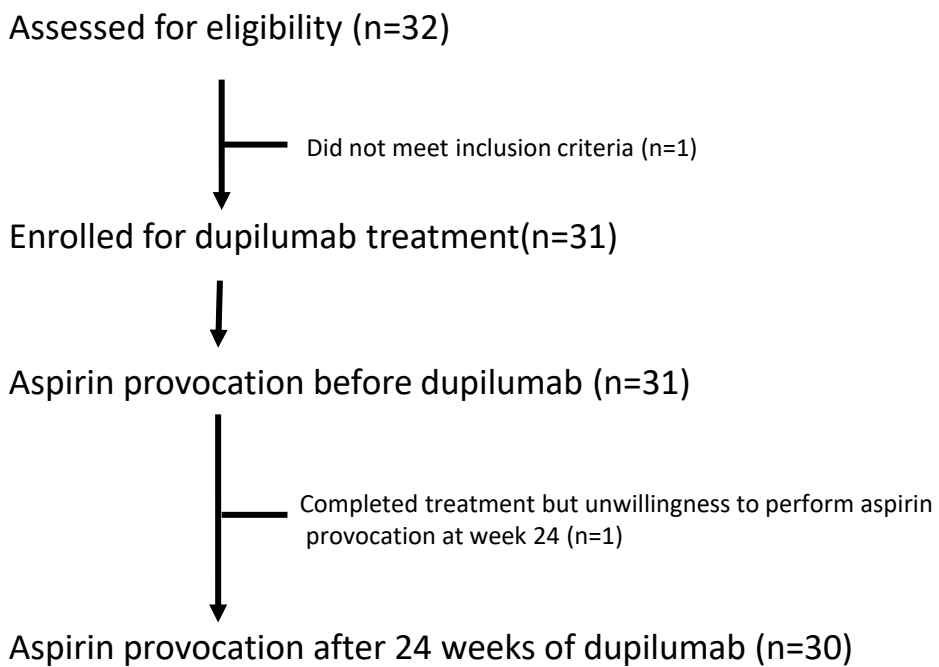
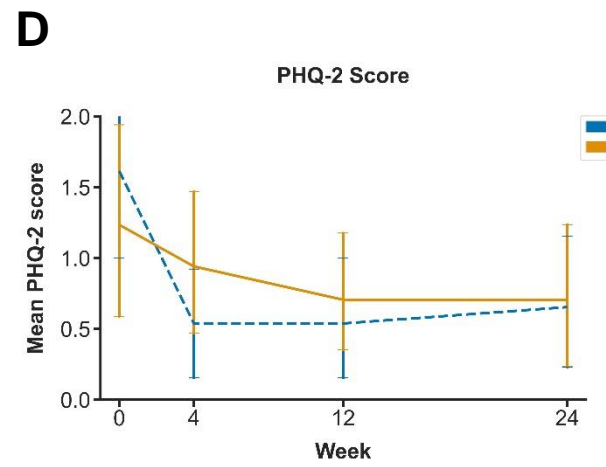
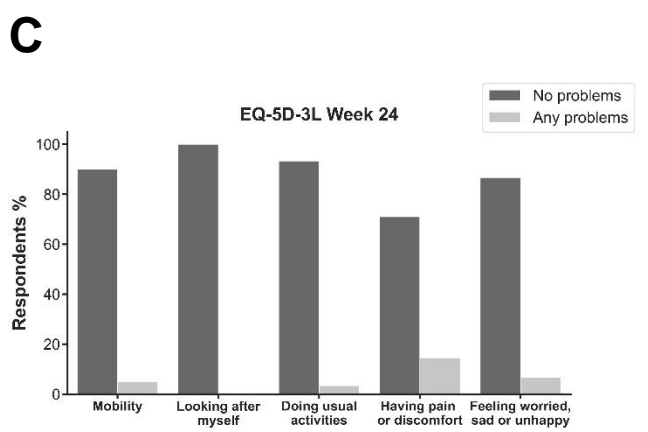
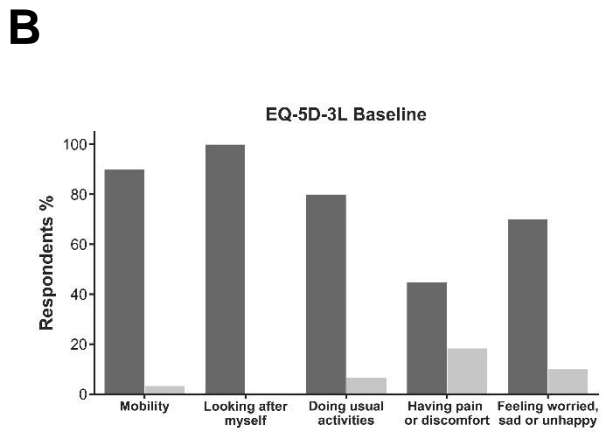
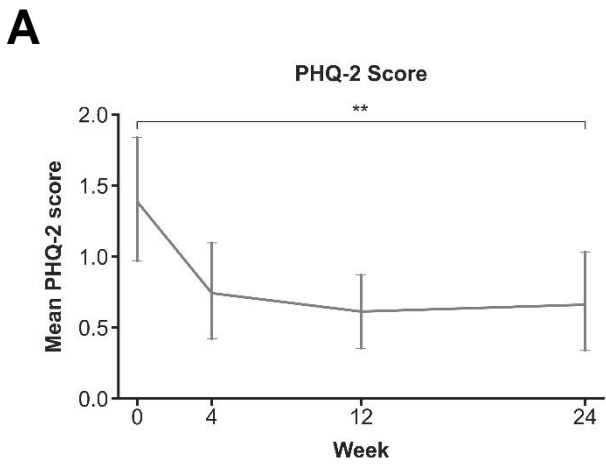


**Figure E1: Study design. (A)** Study design and **(B)** Study flow chart. TPS=total polyp score, TNSS=Total Nasal Symptom Score, SNOT-22=Sino-Nasal Outcome Test-22, UPSIT=University of Pennsylvania Smell Identification Test, QoL=Quality of life scores, ACT=Asthma Control Test.

**A****B**

**Figure E2: Changes in quality of life from baseline over time in N-ERD patients during 24 weeks of dupilumab treatment. (A)** Mean score in PHQ-2 score. **(B-C)** Percentage of respondents in the EQ-5D-3L at **(B)** Baseline and after **(C)** 24 weeks. Dark grey bars represent patients reporting “No problem” and light grey bars “any problem”. **(D)** Mean score in PHQ-2 score in aspirin-tolerant (orange, n=17) and aspirin-intolerant (blue, n=13) patients. Number of patients at each visit and significance of changes between baseline and week 24 are indicated in individual graphs: \*\*p<.01.



**Figure E3: Analysis of selected biomarkers in nasal secretions of N-ERD patients in response to dupilumab treatment.** Boxplots showing levels (pg/mL) of **(A)** G-CSF, **(B)** GM-CSF, **(C)** IFN- $\gamma$ , **(D)** IL-1RA, **(E)** IL-1 $\alpha$ , **(F)** IL-1 $\beta$ , **(G)** IL-2, **(H)** IL-3, **(I)** IL-4, **(J)** IL-7, **(K)** IL-8, **(L)** IL-9, **(M)** IL-10, **(N)** IL-12p70, **(O)** IL-15, **(P)** IL-16, **(Q)** IL-17E/IL-25, **(R)** IL-21, **(S)** IL-27, **(T)** IL-33, **(U)** TNF- $\beta$ , and **(V)** VEGF levels in N-ERD patients (n=31) are displayed at baseline and after 24 weeks of dupilumab treatment. Line within each box represents the median, bottom border represents the 25<sup>th</sup> percentile and top border the 75<sup>th</sup> percentile of the data. Whiskers extend 1.5 times the interquartile range and diamond shaped points are outliers. Significance of changes between baseline and week 24 are indicated in individual graphs: ns=not significant.

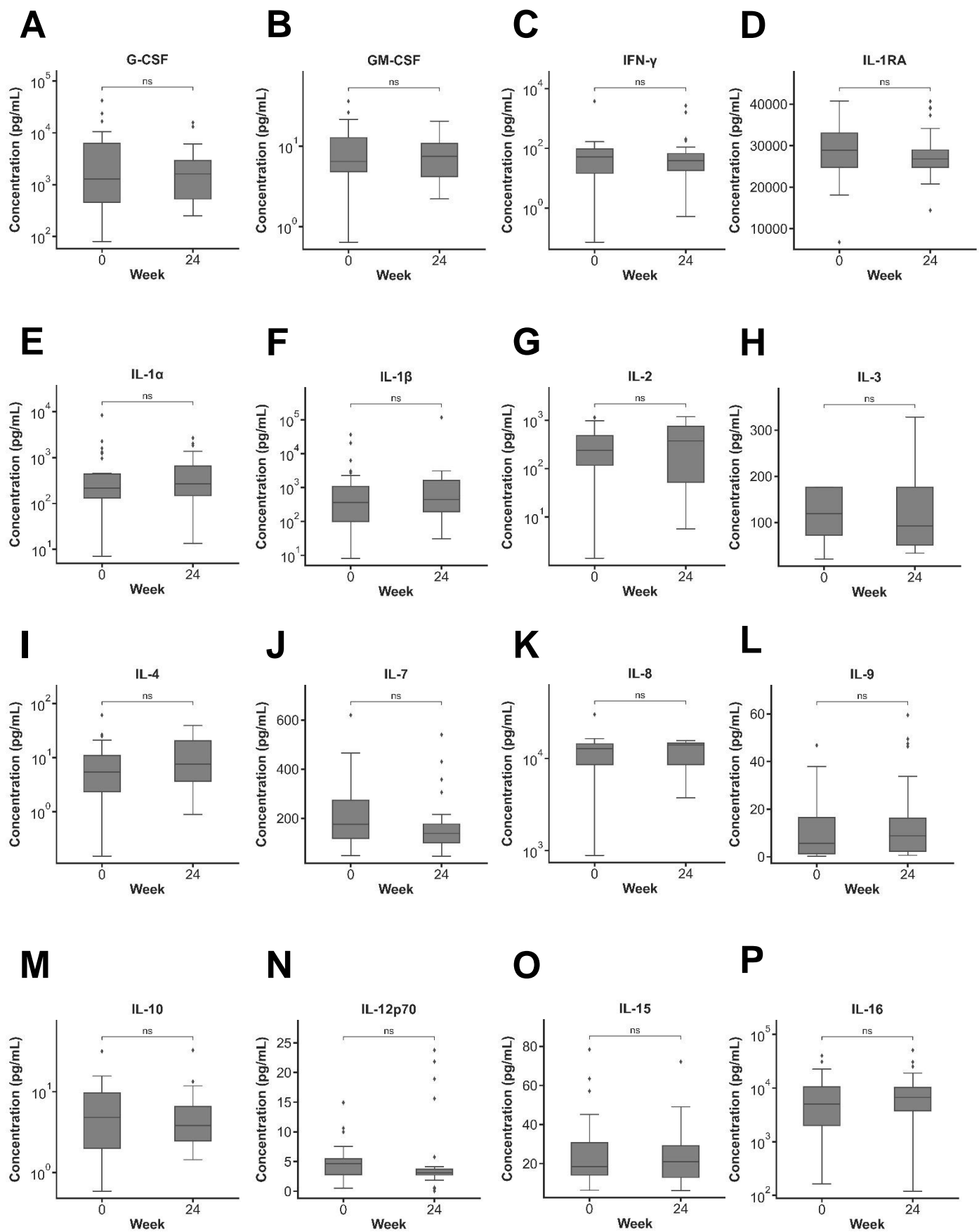
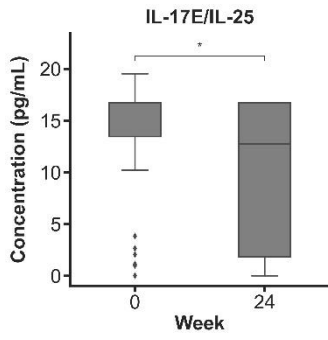
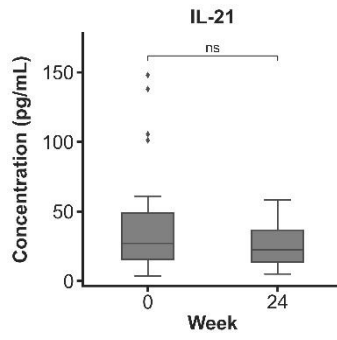
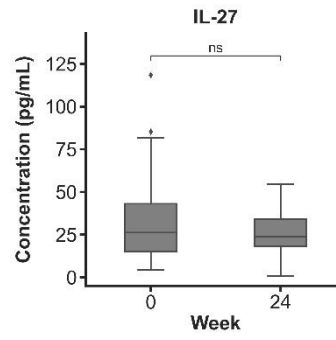
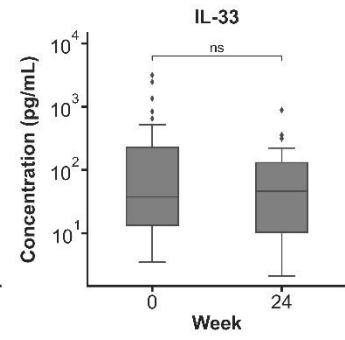
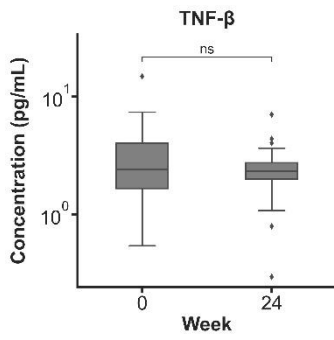
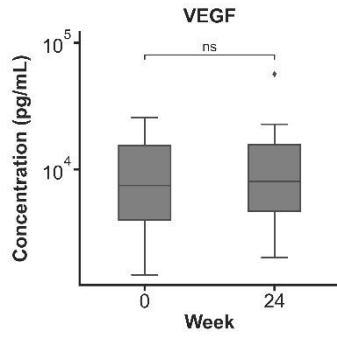


Figure E3

**Q****R****S****T****U****V**

**Figure E4: Analysis of nasal secretion biomarkers in aspirin-tolerant and aspirin-intolerant N-ERD-patients after 24 weeks of dupilumab treatment.**

Boxplots representing levels (pg/mL) of **(A)** Eotaxin-1, **(B)** Eotaxin-3, **(C)** CCL17, **(D)** TNF- $\alpha$ , **(E)** TSLP, **(F)** IL-5, **(G)** IL-6, **(H)** IL-12p40, **(I)** IL-15, **(J)** IL-17A, **(K)** IL-17E/IL-25, **(L)** IL-22, **(M)** G-CSF, **(N)** GM-CSF, **(O)** IFN- $\gamma$ , **(P)** IL-1RA, **(Q)** IL-1 $\alpha$ , **(R)** IL-1 $\beta$ , **(S)** IL-2, **(T)** IL-3, **(U)** IL-4, **(V)** IL-7, **(W)** IL-8, **(X)** IL-9, **(Y)** IL-10, **(Z)** IL-12p70, **(AA)** IL-13, **(AB)** IL-16, **(AC)** IL-21, **(AD)** IL-27, **(AE)** IL-33, **(AF)** TNF- $\beta$  and **(AG)** VEGF levels in N-ERD patients (n=31) are displayed at baseline and after 24 weeks of dupilumab treatment in aspirin-tolerant (orange) or aspirin-intolerant (blue) patients. Line within each box represents the median, bottom border represents the 25<sup>th</sup> percentile and top border the 75<sup>th</sup> percentile of the data. Whiskers extend 1.5 times the interquartile range and diamond shaped points are outliers. Significance of changes between baseline and week 24 are indicated in individual graphs: \*p<.05, \*\*p<.01, \*\*\*p<.001, ns=not significant.



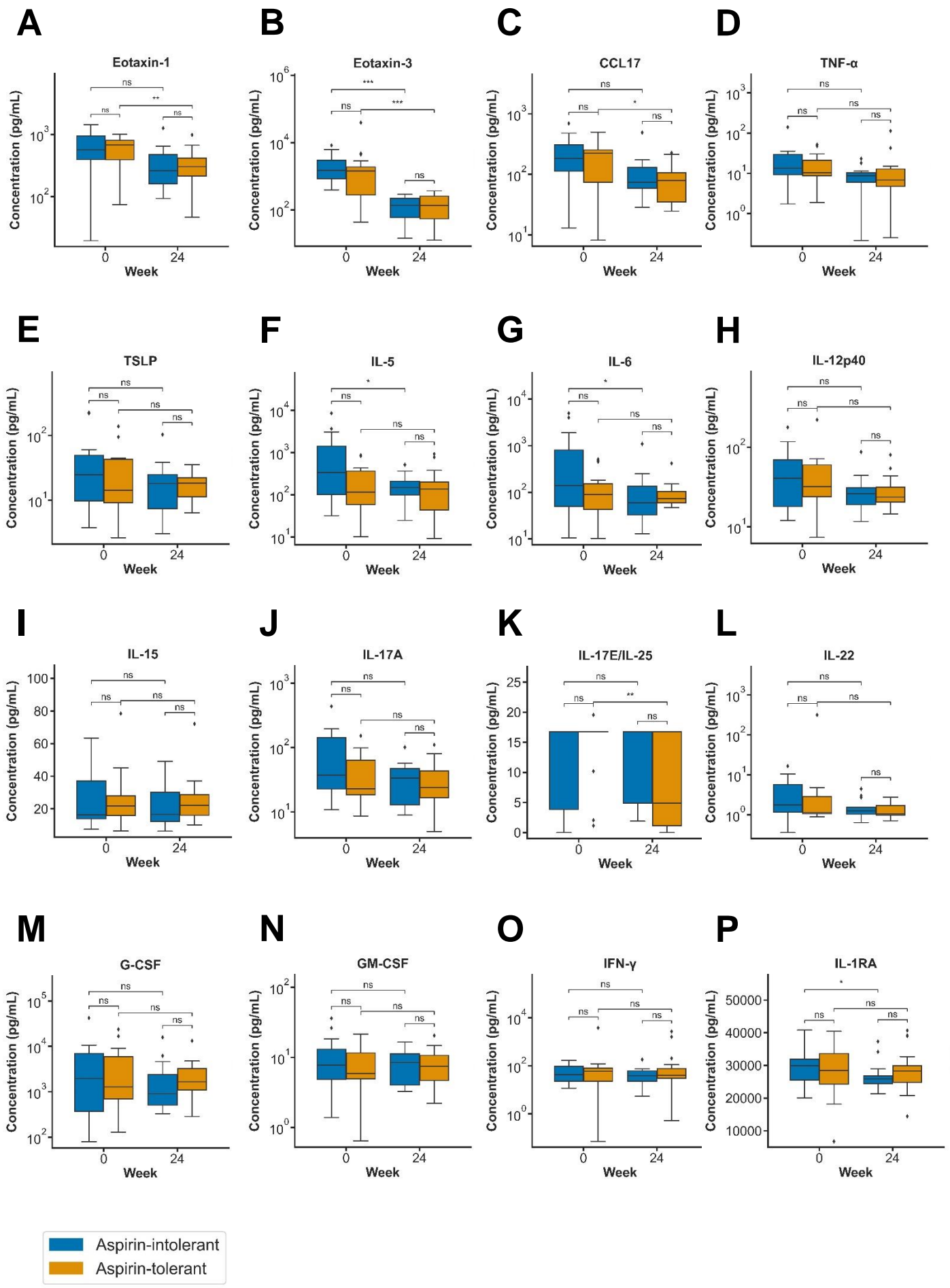


Figure E4

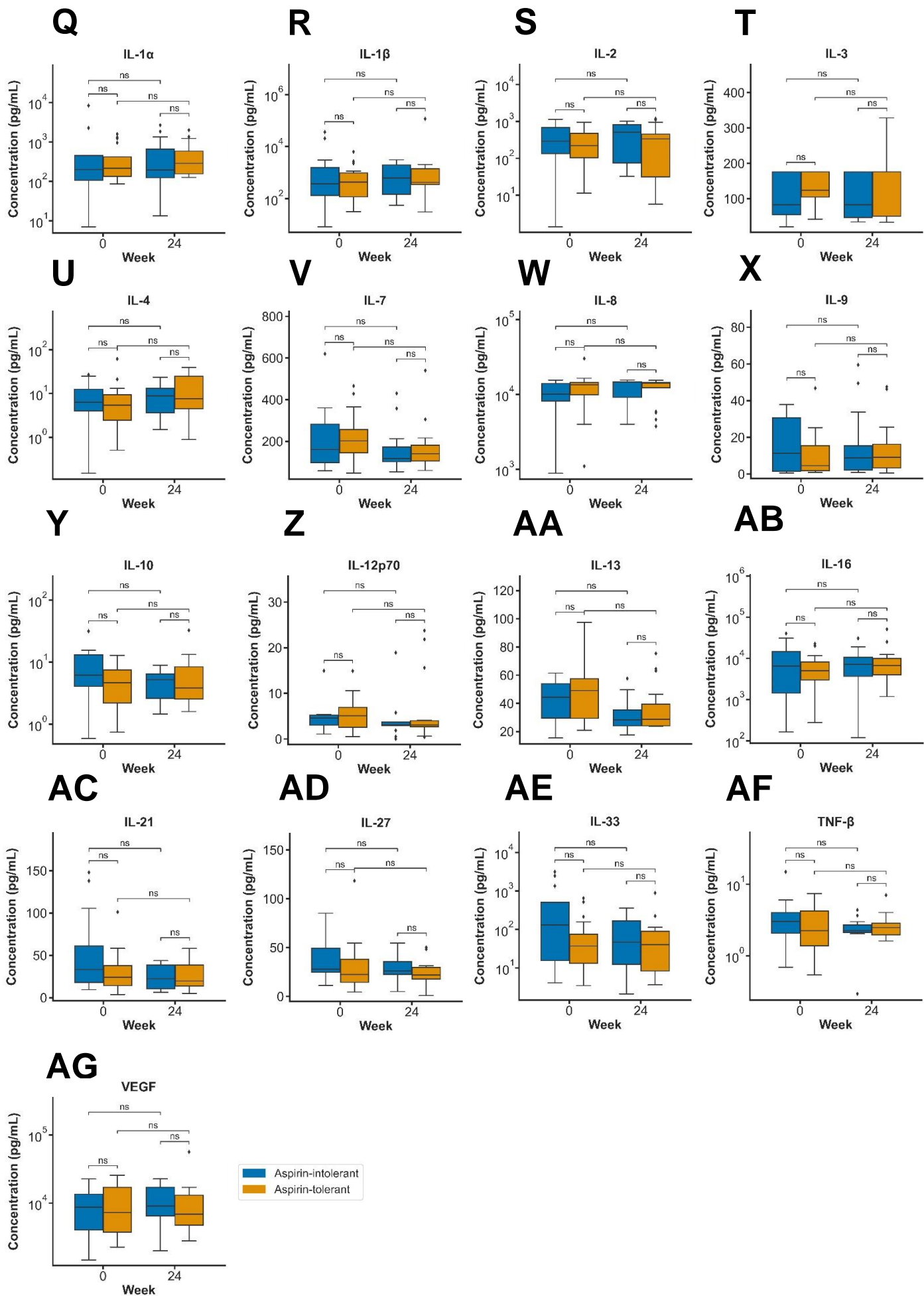
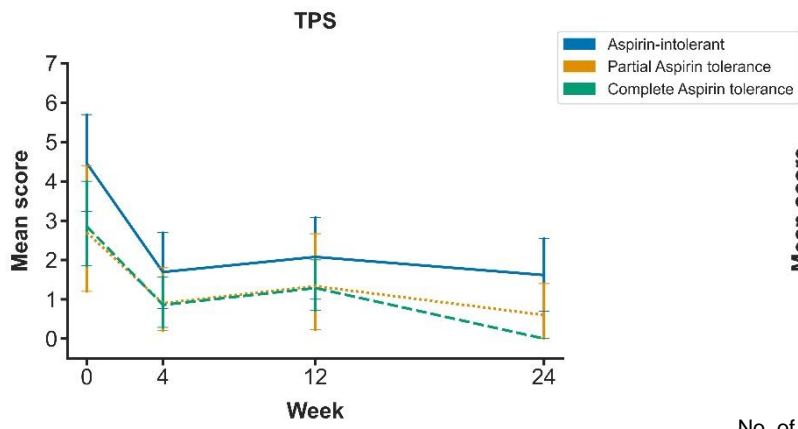
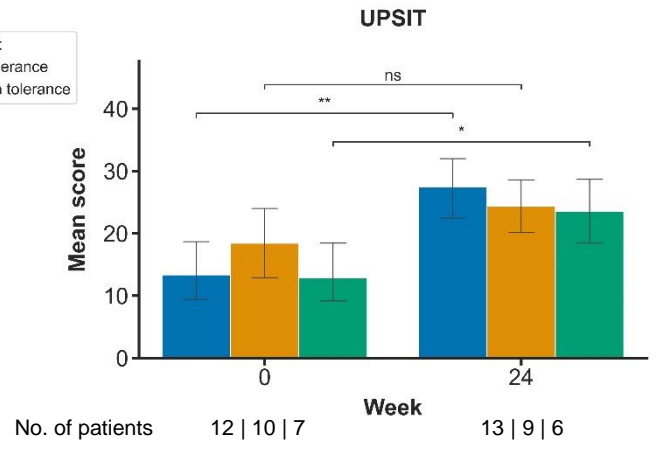
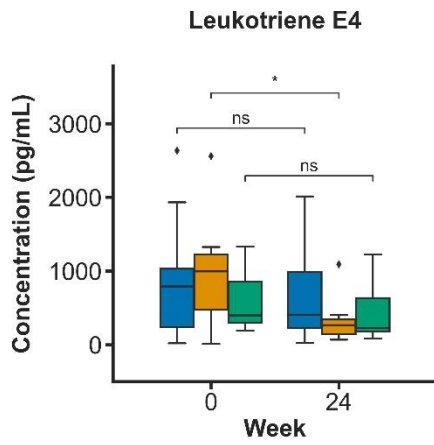
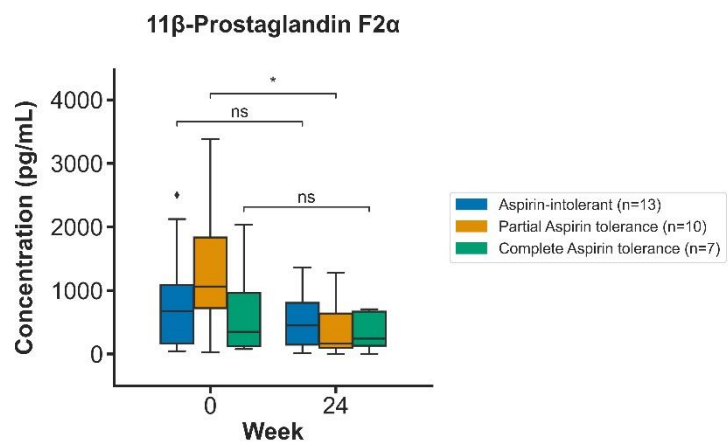


Figure E4

**Figure E5: Analysis of clinical responses, urine, and nasal secretion biomarkers in complete and partial aspirin-tolerant as well as aspirin-intolerant N-ERD-patients after 24 weeks of dupilumab treatment.** Change over time of **(A)** TPS represented as mean score. **(B)** University of Pennsylvania Smell Identification Test (UPSIT) mean score before and after 24 weeks of treatment. **(C-D)** Boxplots representing **(C)** urine 11 $\beta$ -Prostaglandin F<sub>2</sub> $\alpha$  (pg/mL) and **(D)** urine Leukotriene E<sub>4</sub> levels (pg/mL). Data are presented from complete (green) or partial (orange) aspirin tolerant as well as aspirin intolerant (blue) patients. Line within each box represents the median, bottom border represents the 25<sup>th</sup> percentile and top border the 75<sup>th</sup> percentile of the data. Whiskers extend 1.5 times the interquartile range and diamond shaped points are outliers. Significance of changes between baseline and week 24 are indicated in individual graphs: \*p<.05, \*\*p<.01, ns=not significant.

**A****B****Urine****C****D**

**Figure E6: Analysis of nasal secretion biomarkers complete and partial aspirin-tolerant as well as aspirin-intolerant N-ERD-patients after 24 weeks of dupilumab treatment.** Boxplots representing levels (pg/mL) of **(A)** Eotaxin-1, **(B)** Eotaxin-3, **(C)** CCL17, **(D)** TNF- $\alpha$ , **(E)** TSLP, **(F)** IL-5, **(G)** IL-6, **(H)** IL-12p40, **(I)** IL-15, **(J)** IL-17A, **(K)** IL-17E/IL-25, **(L)** IL-22, **(M)** G-CSF, **(N)** GM-CSF, **(O)** IFN- $\gamma$ , **(P)** IL-1RA, **(Q)** IL-1 $\alpha$ , **(R)** IL-1 $\beta$ , **(S)** IL-2, **(T)** IL-3, **(U)** IL-4, **(V)** IL-7, **(W)** IL-8, **(X)** IL-9, **(Y)** IL-10, **(Z)** IL-12p70, **(AA)** IL-13, **(AB)** IL-16, **(AC)** IL-21, **(AD)** IL-27, **(AE)** IL-33, **(AF)** TNF- $\beta$  and **(AG)** VEGF levels are displayed at baseline and after 24 weeks of dupilumab treatment in N-ERD patients (n=31) with complete (green) or partial (orange) aspirin tolerance as well as aspirin intolerant patients (blue) after treatment. Line within each box represents the median, bottom border represents the 25<sup>th</sup> percentile and top border the 75<sup>th</sup> percentile of the data. Whiskers extend 1.5 times the interquartile range and diamond shaped points are outliers. Significance of changes between baseline and week 24 are indicated in individual graphs: \*p<.05, \*\*p<.01, \*\*\*p<.001, ns=not significant.

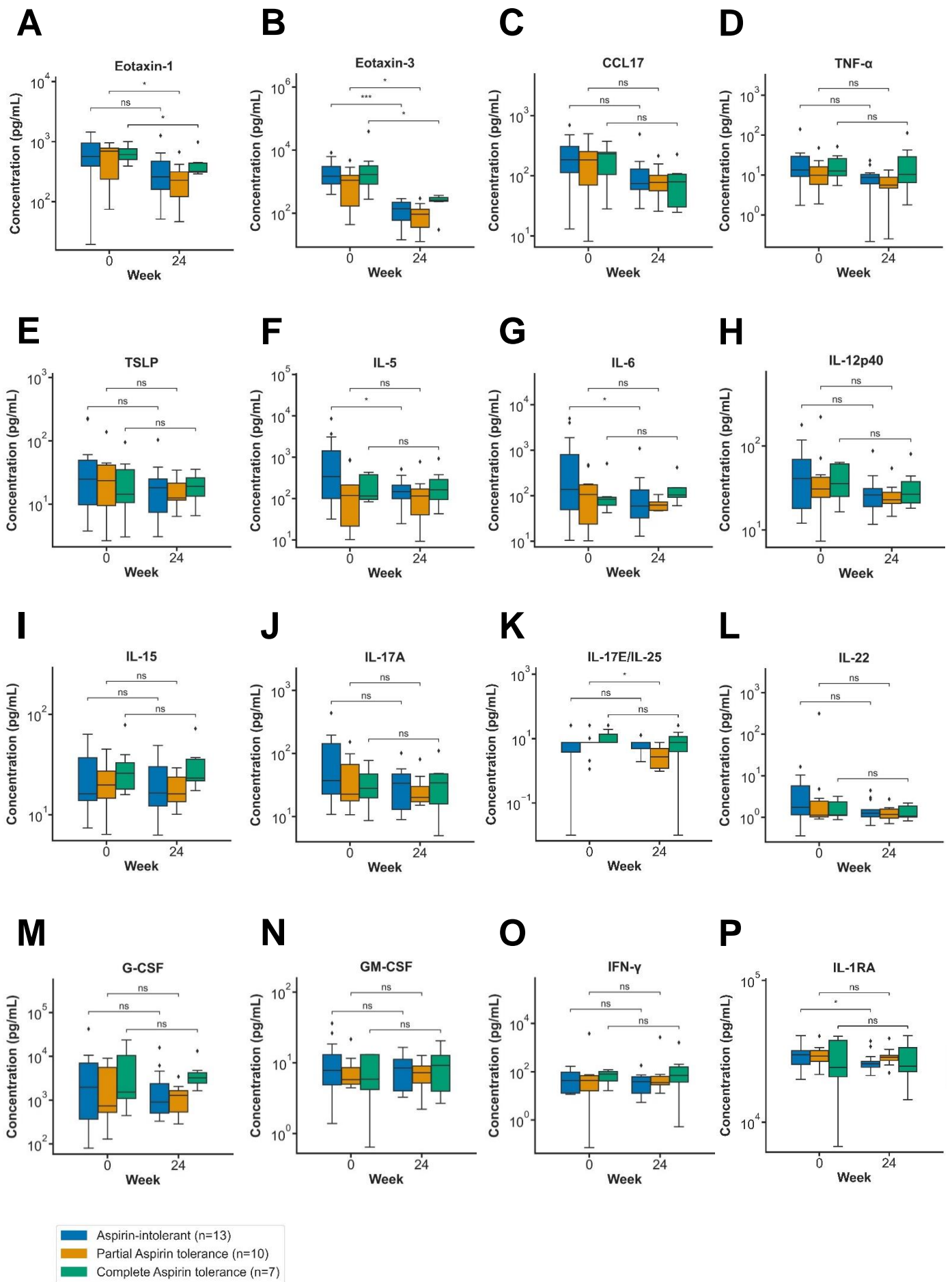


Figure E6

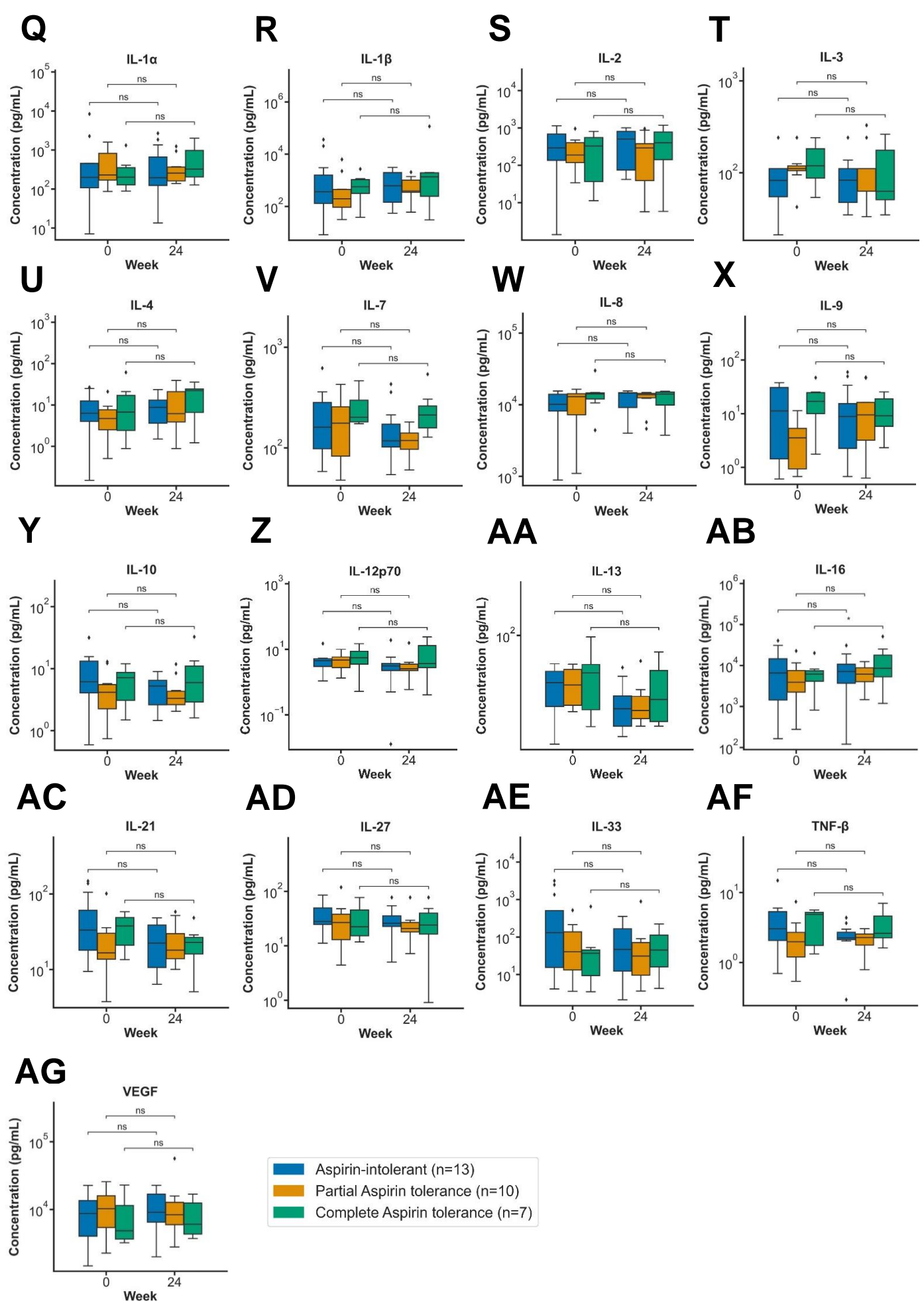


Figure E6