ONLINE RESOURCES

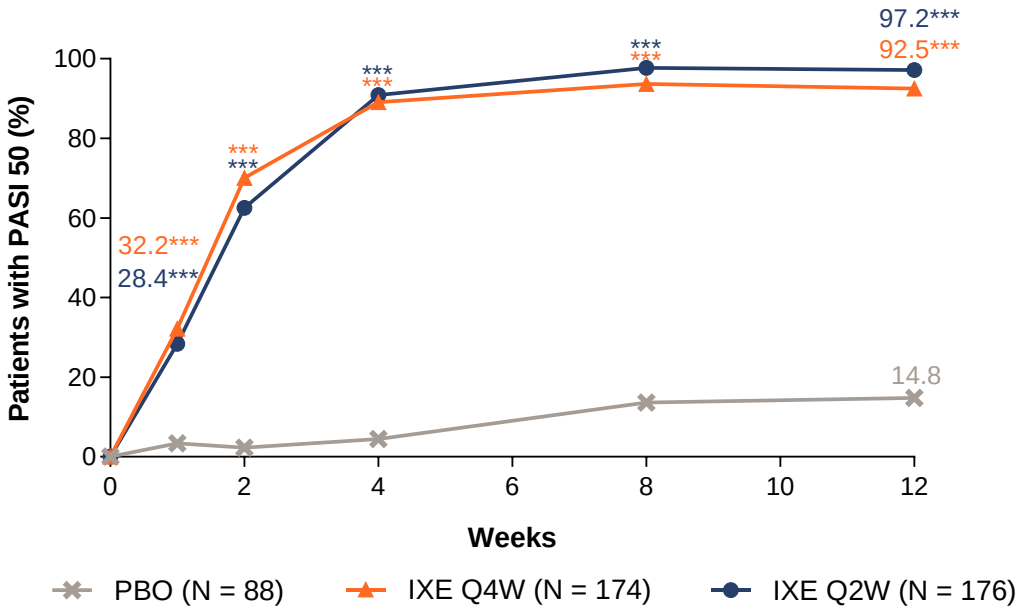
Gatekeeping testing strategy for the primary and major secondary analyses

Tests 1–10 denote the 10 statistical tests that were multiplicity controlled:

Primary 1 (test 1)	Proportion of patients with an sPGA (0, 1) at week 12 compared with placebo
Primary 2 (test 2)	Proportion of patients with PASI 75 at week 12 compared with placebo
Secondary 1 (test 3)	Proportion of patients achieving an sPGA (0) at week 12 compared with placebo
Secondary 2 (test 4)	Proportion of patients with PASI 90 at week 12 compared with placebo
Secondary 3 (test 5)	Proportion of patients with PASI 100 at week 12 compared with placebo
Secondary 4 (test 6)	Proportion of patients maintaining an sPGA (0,1) from week 12 after re-randomization at start of the maintenance dosing period to week 60 compared with placebo for ixekizumab-treated patients who had an sPGA (0,1) at week 12 and were re-randomized
Secondary 5 (test 7)	Proportion of patients maintaining or achieving an sPGA (0) from week 12 after re-randomization at the start of the maintenance dosing period to week 60 compared with placebo for ixekizumab-treated patients who had an sPGA (0,1) at week 12 and were re-randomized
Secondary 6 (test 8)	Proportion of patients achieving an Itch NRS ≥ 4-point reduction from baseline at week 12 compared with placebo (for patients who had baseline Itch NRS ≥ 4)
Secondary 7 (test 9)	Change from baseline in DLQI at week 12 compared with placebo
Secondary 8 (test 10)	Change from baseline in NAPSI (for fingernails) at week 12 compared with placebo

The 10 statistical tests were grouped into two parallel branches according to the dose levels in the induction dosing period. The first branch includes tests of IXE Q2W versus placebo in the induction dosing period, as well as IXE Q2W/IXE Q4W versus IXE Q2W/placebo in the maintenance dosing period. The second branch includes tests of IXE Q4W versus placebo in the induction dosing period, as well as IXE Q4W/IXE Q4W versus IXE Q4W/placebo in the maintenance dosing period. Test 1 was carried out using the Bonferroni procedure (i.e., each dose was tested at a two-sided $\alpha = 0.025$ level). Test 2 was performed at a dose only if test 1 of that dose was significant. Similarly, each test for a particular dose was performed only if all prior tests of that dose were significant. For each dose, if a test was not significant, all subsequent tests were not significant.

Online Resource 1 Time course of PASI 50 response during the induction dosing period. Included patients in the Intention-to-Treat Population; all randomized patients, regardless of whether the patient followed the treatment protocol. Missing data were imputed using non-responder imputation; logistic regression was used. Abbreviations: IXE Q2W=80 mg ixekizumab every 2 weeks, IXE Q4W=80 mg ixekizumab every 4 weeks, PASI=Psoriasis Area and Severity Index, PBO=placebo

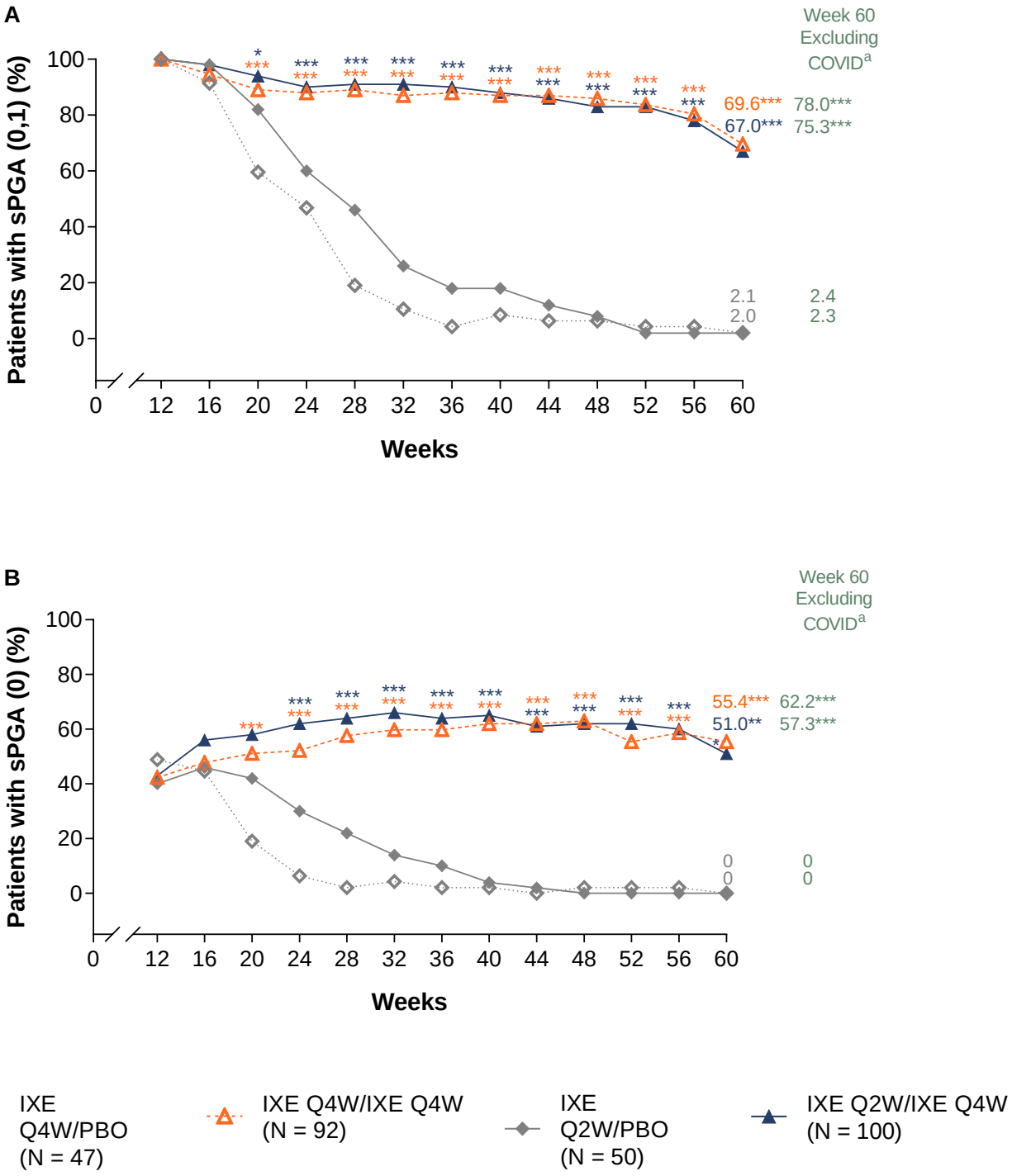


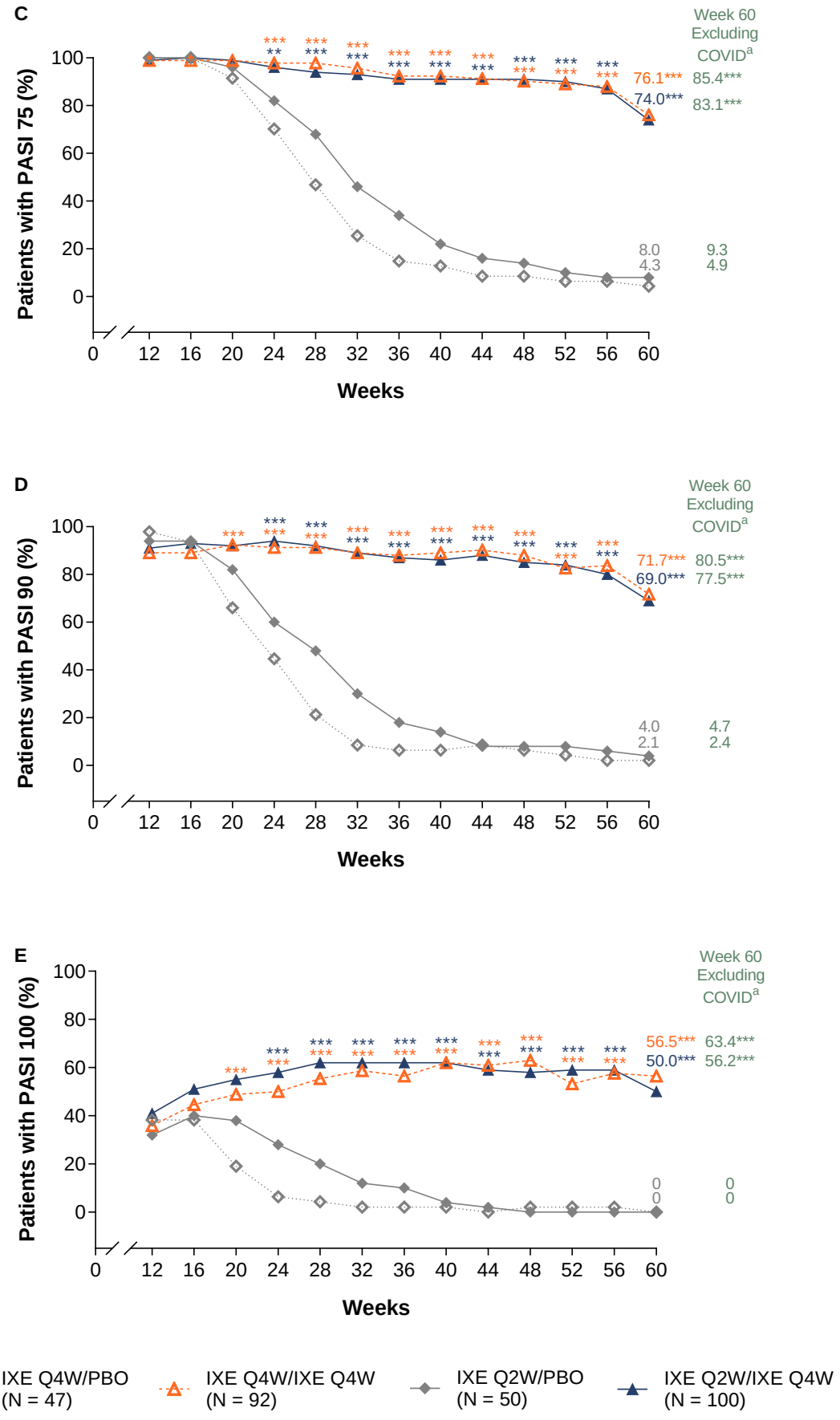
Online Resource 2 Time course of patient responses during the maintenance dosing period (weeks 12–60) for the Maintenance Dosing Primary Population: **a** Percentage of patients with sPGA of 0 (clear) or 1 (minimal psoriasis). **b** Percentage of patients with sPGA (0). **c** Percentage of patients with PASI 75. **d** Percentage of patients with PASI 90. **e** Percentage of patients with PASI 100. Included patients in the Maintenance Dosing Period Primary Population; all patients randomized to ixekizumab during the induction dosing period who achieved sPGA (0,1) at week 12, were re-randomized, and received ≥ 1 dose of study treatment during the maintenance dosing period

Note: for patients with missing visits owing to the COVID-19 pandemic, data from any missing visit week were treated as missing and the patient data for the rest of the maintenance dosing period were included. Missing data were imputed using non-responder imputation and logistic regression was used. In cases where a logistic regression model did not produce results owing to sparse data, the Fisher exact test was used. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ versus IXE Q4W/PBO or IXE Q2W/PBO

[a] Week 60 response rate when patients who had missing measures owing to the COVID-19 pandemic were excluded

Abbreviations: IXE Q2W=80 mg ixekizumab every 2 weeks, IXE Q4W=80 mg ixekizumab every 4 weeks, PASI=Psoriasis Area and Severity Index, PBO=placebo, sPGA=static Physician's Global Assessment


A
Patients with sPGA (0,1) (%)
100
80
60
40
20
0
0
12
16
20
24
28
32
36
40
44
48
52
56
60
Weeks
Week 60 Excluding COVID[a]
69.6***
78.0***
67.0***
75.3***
2.1
2.4
2.0
2.3
B
Patients with sPGA (0) (%)
100
80
60
40
20
0
0
12
16
20
24
28
32
36
40
44
48
52
56
60
Weeks
Week 60 Excluding COVID[a]
55.4***
62.2***
51.0**
57.3***
0
0
0
0
IXE Q4W/PBO (N = 47)
IXE Q4W/IXE Q4W (N = 92)
IXE Q2W/PBO (N = 50)
IXE Q2W/IXE Q4W (N = 100)


C
Patients with PASI 75 (%)
Week 60 Excluding COVID[a]
76.1***
74.0***
85.4***
83.1***
8.0
4.3
9.3
4.9
Weeks
D
Patients with PASI 90 (%)
Week 60 Excluding COVID[a]
71.7***
69.0***
80.5***
77.5***
4.0
2.1
4.7
2.4
Weeks
E
Patients with PASI 100 (%)
Week 60 Excluding COVID[a]
56.5***
50.0***
63.4***
56.2***
0
0
0
0
Weeks
IXE Q4W/PBO (N = 47)
IXE Q4W/IXE Q4W (N = 92)
IXE Q2W/PBO (N = 50)
IXE Q2W/IXE Q4W (N = 100)