Appendix SII

SUPPLEMENTARY RESULTS

All treatment exposure: adverse events with a fatal outcome

A total of 18 treatment-emergent fatal AEs were reported across the 5 trials. In the 12-week induction period, there was 1 fatal AE in the brodalumab 210 mg group, and in the 52-week period there were an additional 4 fatal events: 2 in the brodalumab 210 mg group (event rate per 100 patient-years [E/ 100 PY] 0.7/ 100 PY) and 2 in the ustekinumab group (0.5 /100 PY). The majority of the remaining fatal events occurred in the mixed treatment groups. Many of the fatal events occurred in patients with additional confounding factors relating to prior medical history, concomitant events or the presence of other risk factors (Table SII).

As most of the fatal AEs did not occur in comparable treatment groups, analysis of fatal AEs focused on the mixed treatment group of patients (with their AEs being allocated to the patient's treatment type at the time of the event) ($n=15$) with 0.2 E/100 PY. Actual mortality was compared with expected mortality rate in the general population using sex- and age-adjusted data from the Centers for Disease Control and Prevention (USA), EUROSTAT (Europe) and the WHO (all other countries). The estimated expected number of deaths was 33, which was more than double the number of deaths observed in these studies.

Adverse events of special interest: other psychiatric disorders

During the "while on specified treatment" period, the most frequently observed psychiatric AEs were insomnia, depression and anxiety. AEs associated with depression were observed with 1.6, 1.0, 2.2 and 2.1 E/100 PY while on brodalumab 210 mg, brodalumab 140 mg, ustekinumab and placebo, respectively. AEs associated with anxiety were 1.1, 1.6, 1.4 and 0.8 E/100 PY for those treatment groups, respectively, while mood changes were rare, with only 3 events ("Mood swings" and "Mood altered") recorded in each of 3 patients in the brodalumab 210 mg group (<0.05 E/100 PY). One patient in the brodalumab 140 mg group was recorded as having a mood-swing event. There was no evidence of increased psychiatric AEs in patients treated with brodalumab compared with the other treatment groups.

In the AMAGINE-1 study, scores for depression and anxiety on the Hospital Anxiety and Depression Scale improved, and were significantly lower in, patients treated with brodalumab compared with placebo ($p<0.001$) (11).