Aims: New insulin glargine U300 (Gla-300, 300 U/mL) has even flatter and more prolonged PK and PD profiles than insulin glargine 100 U/mL (Gla-100). EDITION 1 compared efficacy and safety of Gla-300 vs Gla-100 in T2DM using mealtime+basal insulin. Methods: In this multicentre, open-label, phase 3a, 6-month study, 807 participants were randomised (1:1) to Gla-300 or Gla-100 once daily in the evening. Primary endpoint was change in HbA1c, baseline to 6 months; first main secondary efficacy endpoint was participants (%) with ≥1 confirmed or severe (≤3.9 mmol/l) nocturnal (0000–0559 h) hypoglycaemia week 9–month 6. Results: Gla-300 was non-inferior to Gla-100 for change in HbA1c, LS mean change −0.83 (SE 0.06) % in both groups at 6 months, difference −0.00 (95%CI: −0.11−0.11) %. Significantly fewer participants experienced confirmed or severe nocturnal hypoglycaemia (week 9–month 6) with Gla-300 compared with Gla-100 (146 [36.1%] vs 184 [46.0%], RR 0.79 [95%CI: 0.67–0.93]; p=0.005). A similar and consistent reduction was observed during the first 8 weeks (26.2% vs 33.3%, RR 0.79 [95%CI: 0.64–0.98]) and over the whole 6-month treatment period (44.6% vs 57.5%, RR 0.78 [95%CI: 0.68–0.89]). Over the 6-month treatment period the rate of confirmed or severe nocturnal events was lower with Gla-300 than Gla-100 (3.13 vs 4.20 events/person-yr), and the rates of daytime (0600–2359 h) events were similar (22.4 vs 22.6 events/person-yr). Conclusion: Gla-300 provides similarly effective glycaemic control with less confirmed or severe nocturnal hypoglycaemia compared with Gla-100.