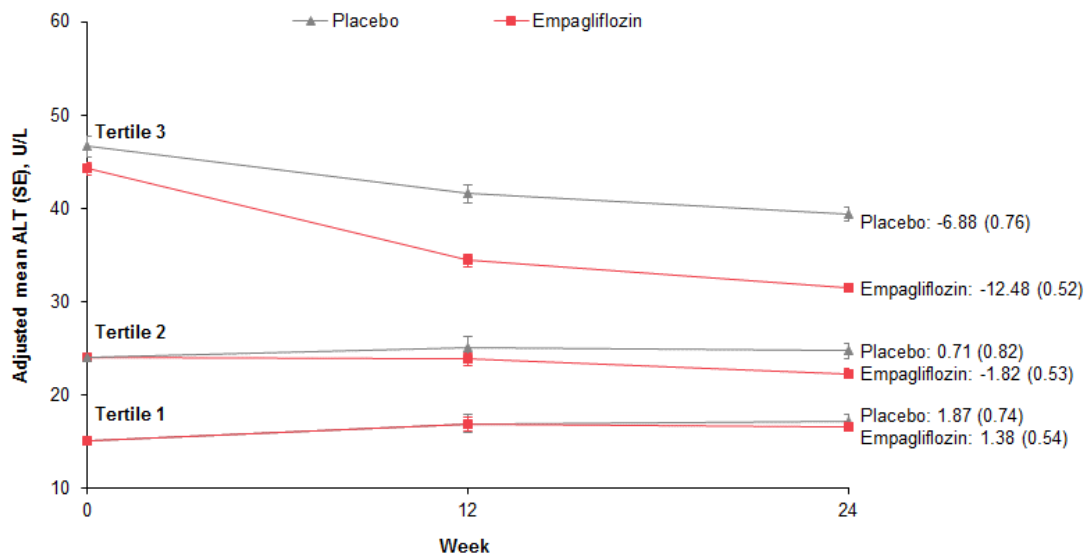**Empagliflozin is associated with improvements in liver enzymes potentially consistent with reductions in liver fat: results from randomised trials including the EMPA-REG OUTCOME® trial (Sattar N et al.)**
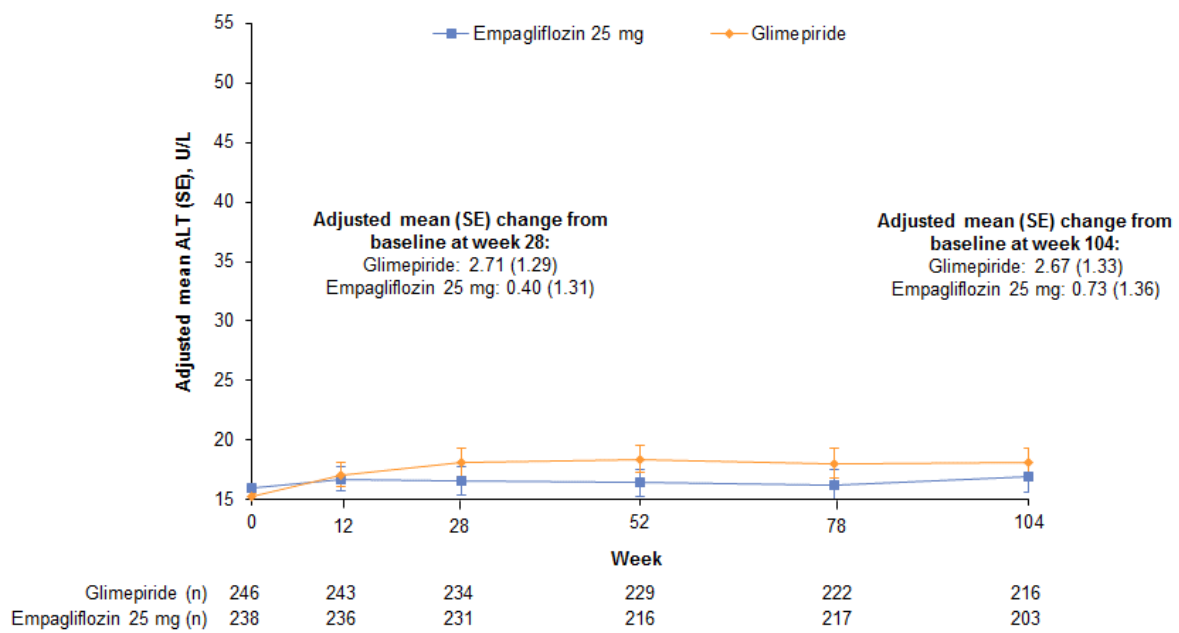
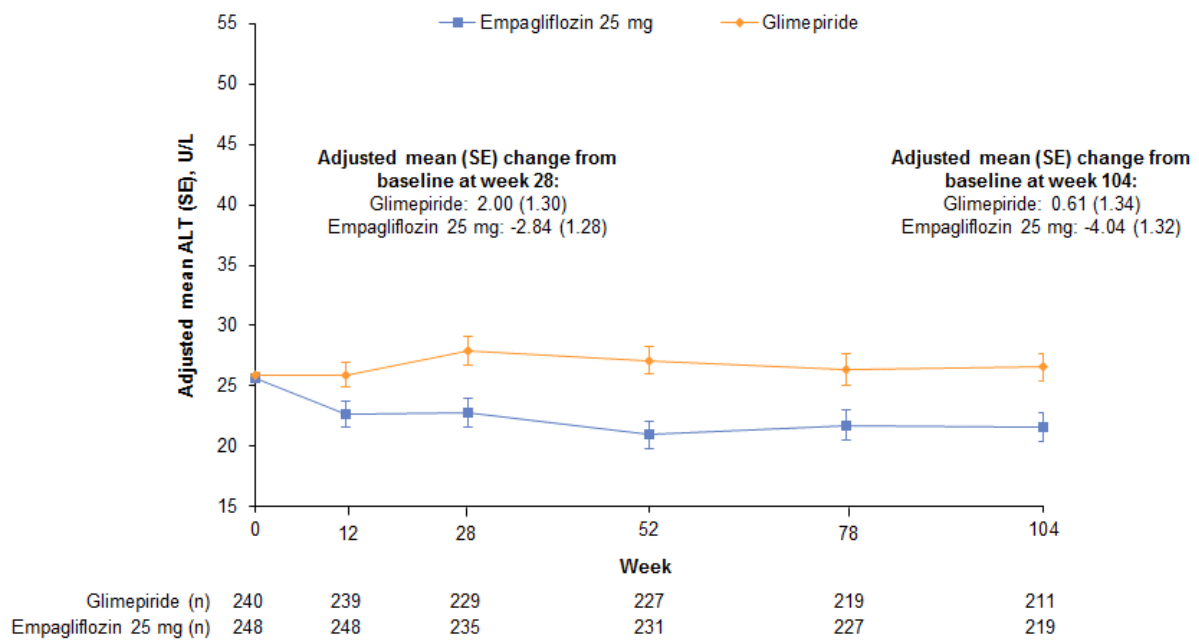**Electronic supplementary material (ESM)**

ESM Figure 1. Changes in alanine aminotransferase (ALT) in pooled 24-week trial data in tertiles by baseline ALT. Mixed model repeated measures analysis in patients treated with ≥1 dose of study drug based on observed cases, including values after initiation of rescue medication. Baseline values are mean (SE). SE, standard error.
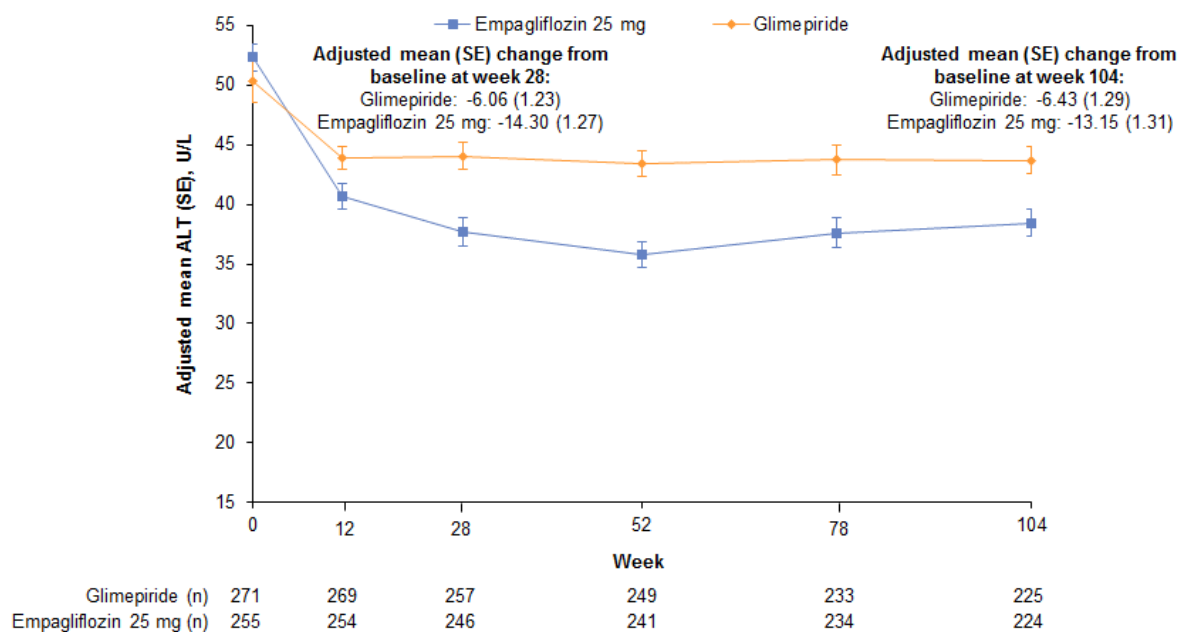
a

Adjusted mean (SE) change from
baseline at week 28:
Glimepiride: 2.71 (1.29)
Empagliflozin 25 mg: 0.40 (1.31)

Adjusted mean (SE) change from
baseline at week 104:
Glimepiride: 2.67 (1.33)
Empagliflozin 25 mg: 0.73 (1.36)

Adjusted mean ALT (SE), U/L

Empagliflozin 25 mg   Glimepiride

Week

Glimepiride (n)	246	243	234	229	222	216
Empagliflozin 25 mg (n)	238	236	231	216	217	203

b

Adjusted mean (SE) change from
baseline at week 28:
Glimepiride: 2.00 (1.30)
Empagliflozin 25 mg: -2.84 (1.28)

Adjusted mean (SE) change from
baseline at week 104:
Glimepiride: 0.61 (1.34)
Empagliflozin 25 mg: -4.04 (1.32)

Adjusted mean ALT (SE), U/L

Empagliflozin 25 mg   Glimepiride

Week

Glimepiride (n)	240	239	229	227	219	211
Empagliflozin 25 mg (n)	248	248	235	231	227	219

c

ESM Figure 2. Changes in alanine aminotransferase (ALT) in the EMPA-REG H2H-SU trial in tertiles of patients by baseline ALT: (**a**) tertile 1; (**b**) tertile 2; (**c**) tertile 3. Mixed model repeated measures analysis in patients treated with ≥1 dose of study drug based on observed cases, including values after initiation of rescue medication. Baseline values are mean (SE). SE, standard error.
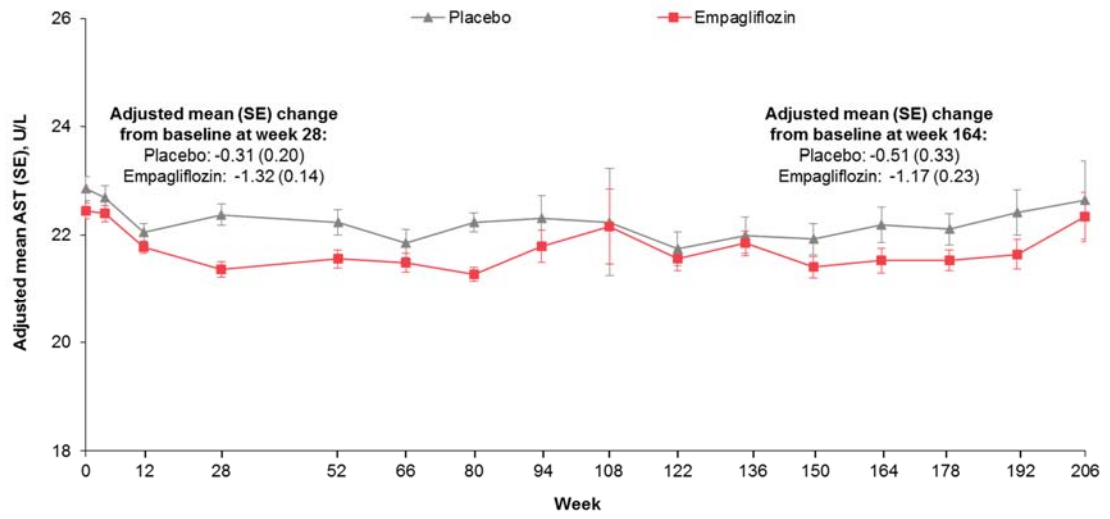
a

Figure shows adjusted mean AST (SE), U/L over weeks for Placebo and Empagliflozin.

Legend: Placebo, Empagliflozin

Adjusted mean (SE) change from baseline at week 28:
Placebo: -0.31 (0.20)
Empagliflozin: -1.32 (0.14)

Adjusted mean (SE) change from baseline at week 164:
Placebo: -0.51 (0.33)
Empagliflozin: -1.17 (0.23)

|	0	12	28	52	66	80	94	108	122	136	150	164	178	192	206
Placebo (n)	2312	2217	2146	2041	1973	1902	1844	1629	1351	1146	1009	877	617	362	129
Empagliflozin (n)	4611	4426	4330	4154	4058	3957	3865	3418	2876	2466	2195	1912	1425	905	330

b
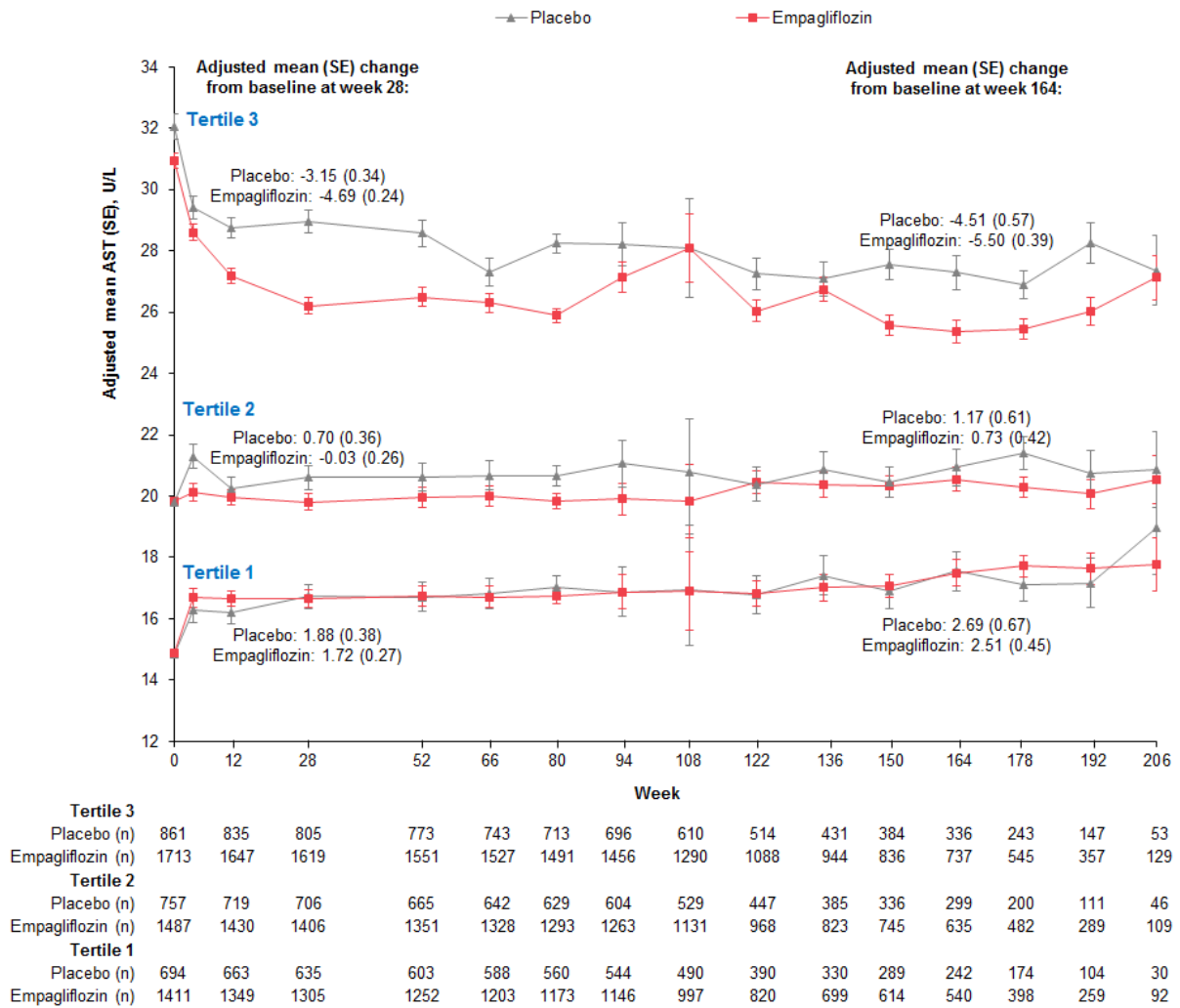
ESM Figure 3. Changes in aspartate aminotransferase (AST) in the EMPA-REG OUTCOME® trial in (**a**) all patients and (**b**) tertiles by baseline AST. Mixed model repeated measures analysis in patients treated with ≥1 dose of study drug based on observed cases, including values after initiation of rescue medication.
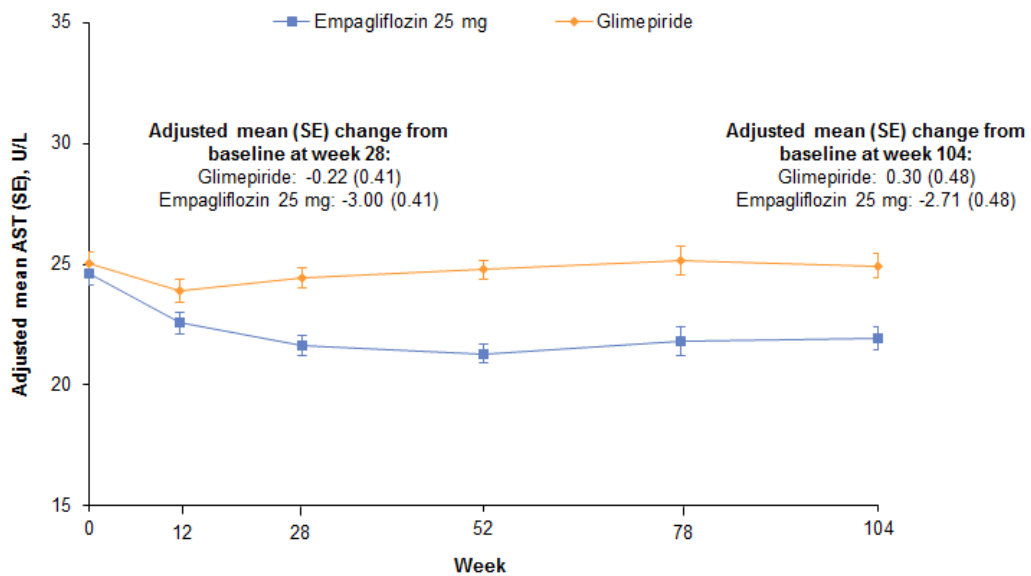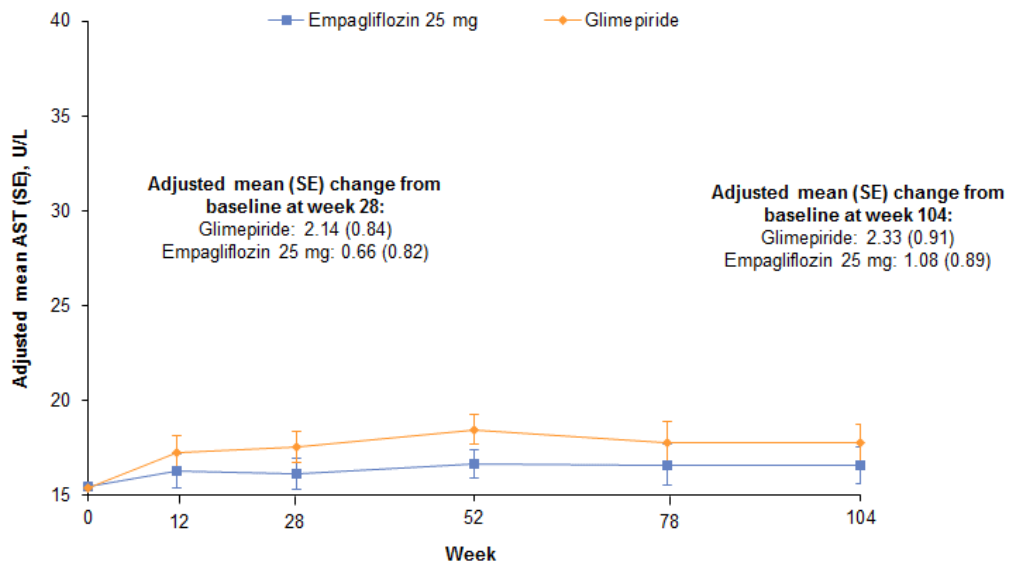
a
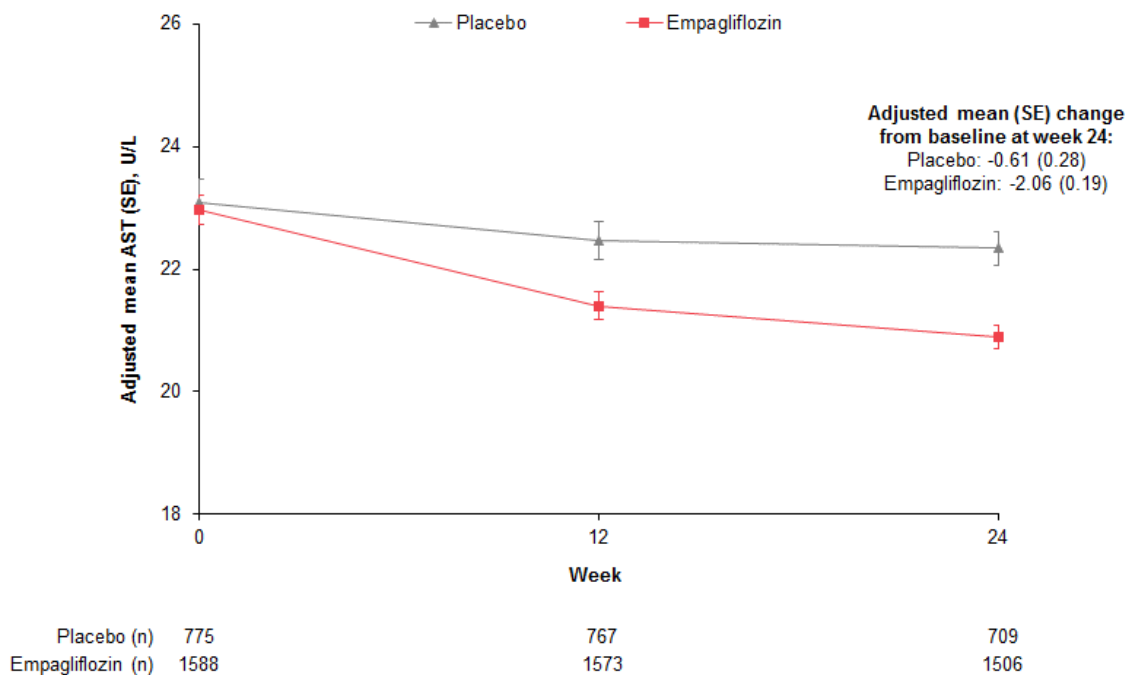
b
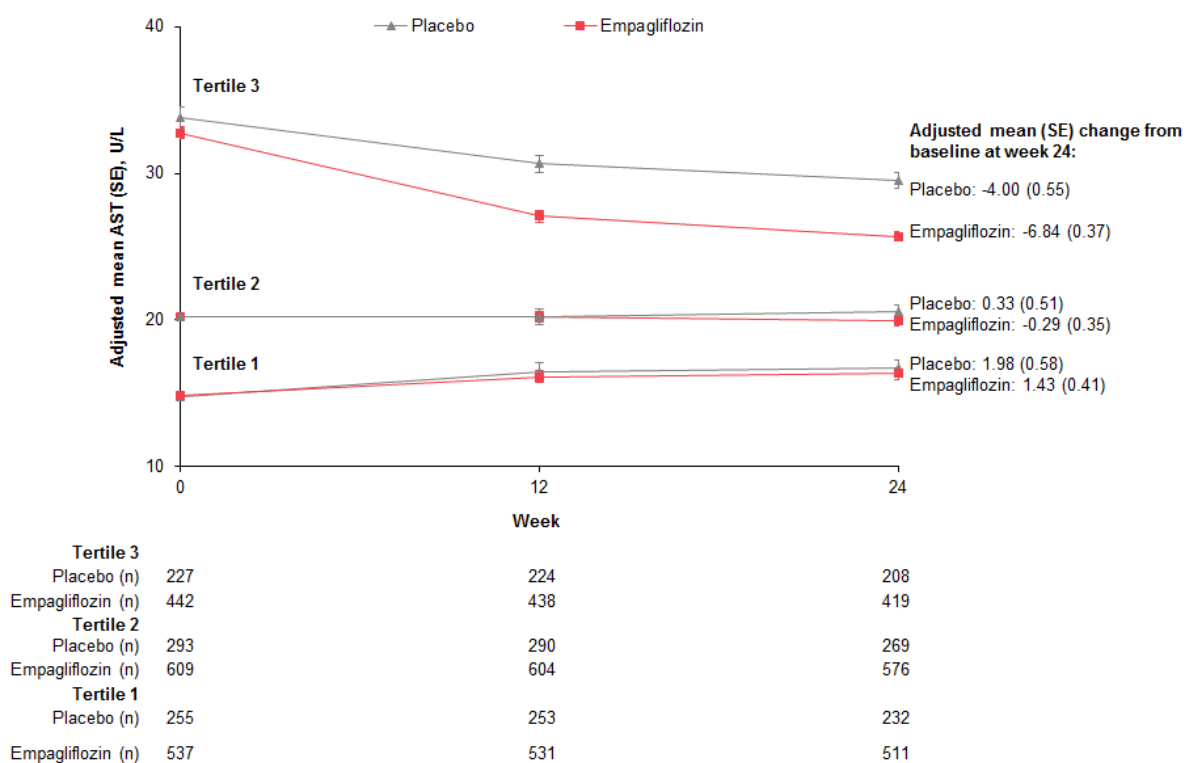
ESM Figure 4. Changes in aspartate aminotransferase (AST) in pooled 24-week trial data in (**a**) all patients and (**b**) tertiles of patients by baseline ALT. Mixed model repeated measures analysis in patients treated with ≥1 dose of study drug based on observed cases, including values after initiation of rescue medication. Baseline values are mean (SE). SE, standard error.
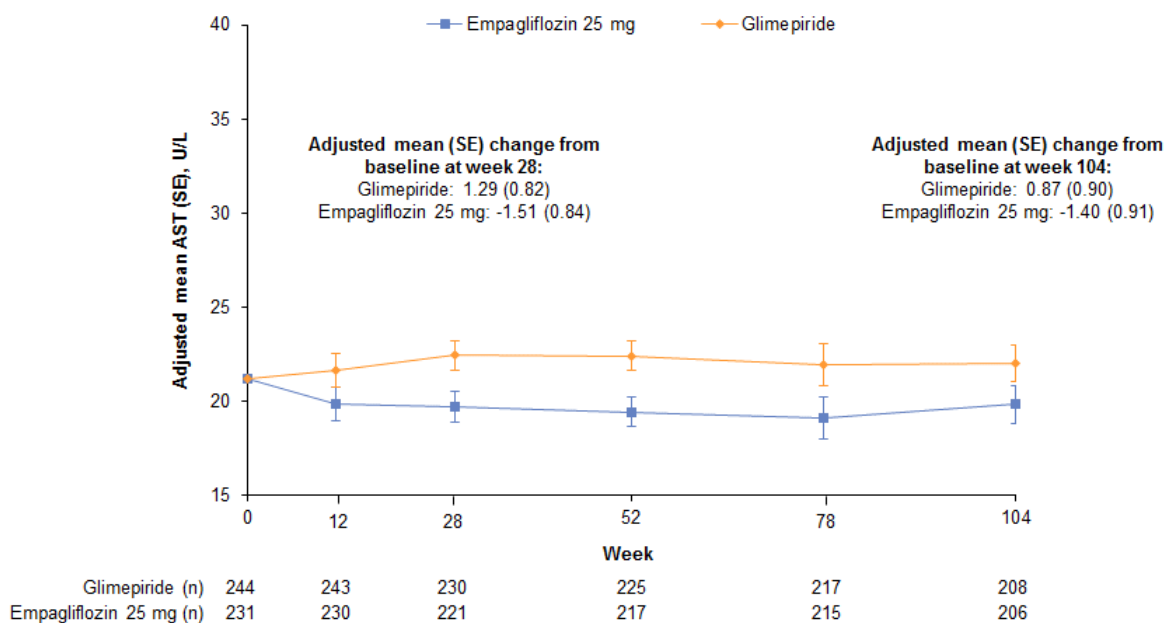
a

b

c

d

ESM Figure 5. Changes in aspartate aminotransferase (AST) in the EMPA-REG H2H-SU trial in (**a**) all patients and in tertiles of patients by baseline ALT: (**b**) tertile 1; (**c**) tertile 2; (**d**) tertile 3. Mixed model repeated measures analysis in patients treated with ≥1 dose of study drug based on observed cases, including values after initiation of rescue medication. Baseline values are mean (SE). SE, standard error