THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

## Abstract Submission No.: A-0742

# Phase II Dose-Selection, Randomised, Controlled Trial of ASi BI 690517 With and Without EMPA in CKD: Subgroup Analysis by T2D Status

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**Objectives :** We investigated efficacy and safety of BI 690517, a novel aldosterone synthase inhibitor (ASI), in people with CKD with or without type 2 diabetes (T2D), and present an analysis by T2D status, pooled for background randomisation to empagliflozin (EMPA) or placebo ($PBO_{EMPA}$).
**Methods :** Trial design is shown in Figure 1.
**Results :** 586 people were randomised at R2; 414 (70.6%) with T2D, and 172 (29.4%) without T2D. Baseline demographics and clinical characteristics were mostly similar between these groups. However, those with T2D had higher mean BMI (30.6 vs 28.3 kg/$m^2$), systolic BP (135.3 vs 130.2 mmHg), eGFR (53.0 vs 49.4 mL/min/1.73$m^2$), and median UACR (444.7 vs 409.2 mg/g) than those without T2D. BI 690517 consistently reduced UACR versus $PBO_{ASI}$ in people with and without T2D (p = 0.38, indicating no between-group difference in treatment effect), with the largest reductions observed in the 10 and 20 mg dose-groups; however, for the 3 mg dose-group, UACR reduction was only observed in people with T2D (Figure 2). UACR response (≥30% reduction in UACR at week 14) was achieved in more than half of people with and without T2D in the BI 690517 10 and 20 mg dose-groups, with the highest response rates in those also receiving EMPA (10 mg dose-group: with T2D, 74.3%; without T2D, 64.0%). Adverse events leading to discontinuation of BI 690517 10 and 20 mg were more common among people with T2D than among those without T2D.
**Conclusions :** In people who had CKD, with or without T2D, BI 690517 dose-dependently reduced UACR, with high rates of UACR response suggestive of additive beneficial effects when given with EMPA.

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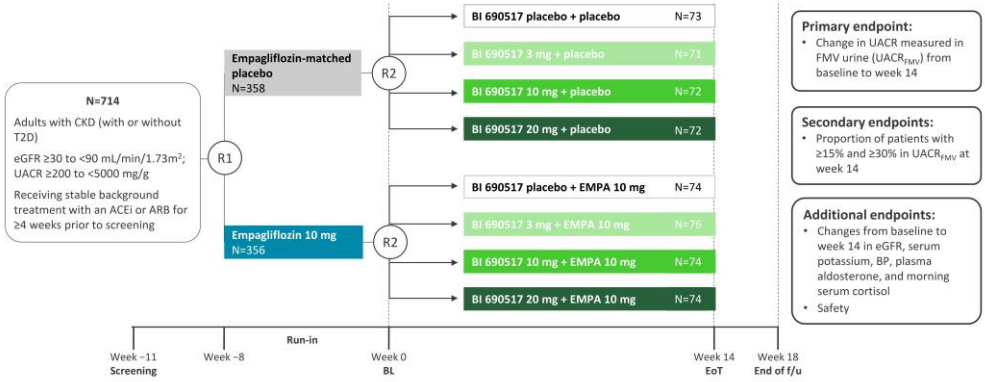
**Figure 1:** Trial design – multinational, phase II, double-blind, dose-selection, randomised controlled trial (NCT05182840)




ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BL, baseline; BP, blood pressure; CKD, chronic kidney disease; EMPA, empagliflozin; eGFR, estimated glomerular filtration rate; EoT, end of treatment; FMV, first morning void; f/u, follow-up; R, randomisation; T2D, type 2 diabetes; UACR, urine albumin:creatinine ratio

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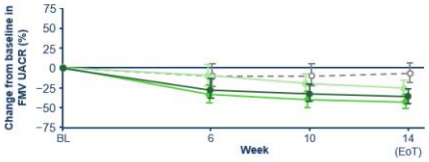
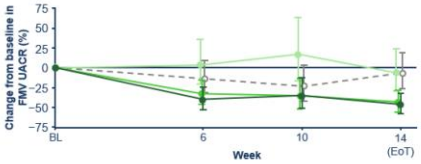
**Figure 2:** Median (95% CI) percentage change from R2 BL in UACR up to Week 14 following BI 690517 treatment in people (A) with and (B) without T2D

A. With T2D




| Change from baseline to week 14 | Median % change in UACR (95% CI) | PBO-corrected change (95% CI) |
|---|---|---|
| Pooled* BI 690517 pbo (n=80) | −6.3 (−18.1, 7.3) | Ref |
| Pooled* BI 690517 3 mg (n=86) | −25.1 (−34.3, −14.6) | −20.1 (−33.8, −3.6) |
| Pooled* BI 690517 10 mg (n=62) | −42.1 (−50.3, −32.6) | −38.2 (−49.6,−24.4) |
| Pooled* BI 690517 20 mg (n=61) | −35.1 (−44.3, −24.5) | −30.8 (−43.5, −15.1) |

B. Without T2D




| Change from baseline to week 14 | Median % change in UACR (95% CI) | PBO-corrected change (95% CI) |
|---|---|---|
| Pooled* BI 690517 pbo (n=40) | −5.8 (−25.8, 19.6) | Ref |
| Pooled* BI 690517 3 mg (n=29) | −5.4 (−28.3, 24.7) | 0.4 (−30.4, 44.7) |
| Pooled* BI 690517 10 mg (n=36) | −42.8 (−55.2, −27.1) | −39.4 (−56.9, −14.7) |
| Pooled* BI 690517 20 mg (n=34) | −46.1 (−58.0, −30.8) | −42.8 (−59.5, −19.2) |

BL, baseline; CI, confidence interval; EoT, end of treatment; FMV, first morning void; T2D, type 2 diabetes; UACR, urine albumin:creatinine ratio
*Pooled groups include participants who received BI 690517, given either alone or in combination with EMPA