# Effects of renal impairment on the pharmacokinetics of dual GIP and GLP-1 receptor agonist Tirzepatide

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**Supplemental Table 1** Subject groups based on renal impairment status

| Classification | eGFR[a], mL/min/1.73m$^2$ | N (MDRD) | N (CKD-EPI) | Creatinine Clearance[b], mL/min | N (Cockroft-Gault) |
|---|---|---|---|---|---|
| **Control (normal renal function)** | ≥90 | 14 | 15 | ≥90 | 17 |
| **Mild renal impairment** | 60–89 | 8 | 7 | 60–89 | 8 |
| **Moderate renal impairment** | 30–59 | 8 | 8 | 30–59 | 6 |
| **Severe renal impairment** | <30 and not requiring dialysis | 7 | 7 | <30 and not requiring dialysis | 6 |
| **End-stage renal disease** | Requiring dialysis | 8 | 8 | Requiring dialysis | 8 |

[a]Groups were classified by eGFR determined using the MDRD abbreviated equation for the primary analysis and additionally reclassified using eGFR calculated by the CKD-EPI equation for an exploratory analysis.

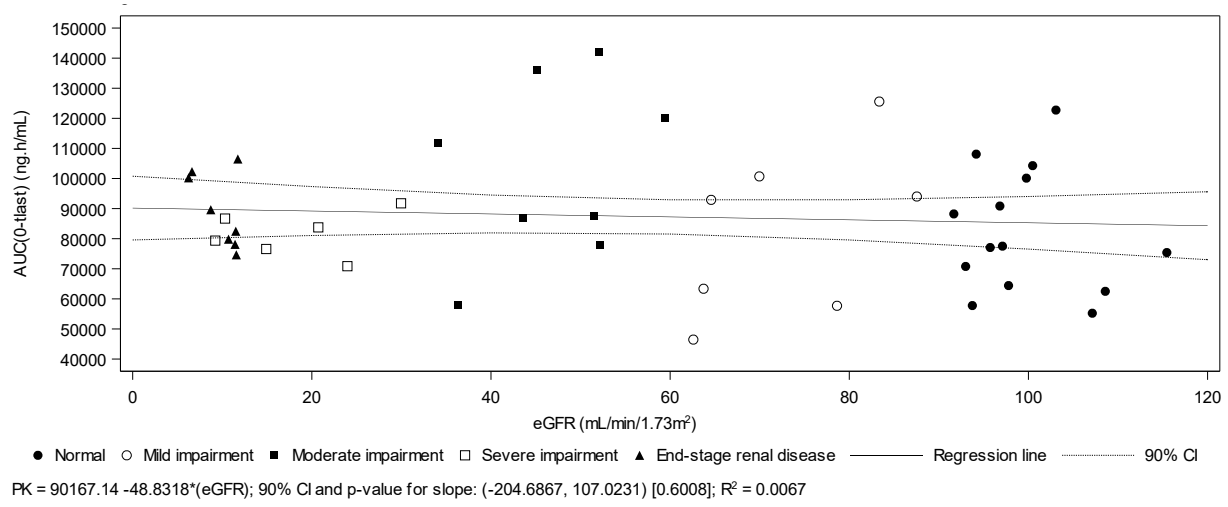
[b]Groups were reclassified using creatinine clearance determined by the Cockcroft-Gault equation for an exploratory analysis.

*CKD-EPI* Chronic Kidney Disease Epidemiology Collaboration, *eGFR* estimated glomerular filtration rate, *MDRD* Modification of Diet in Renal Disease, *N* number of subjects in each renal classification.

**Supplemental Fig. 1** Relationship between pharmacokinetic parameters of tirzepatide 5 mg and renal function calculated by CKD-EPI eGFR

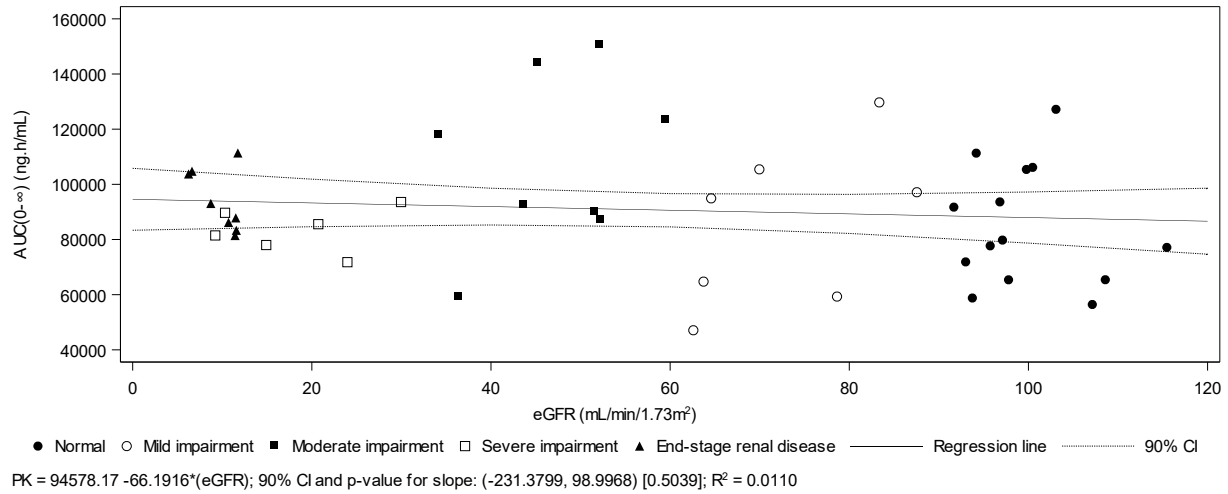
$AUC_{\infty}$ area under the plasma concentration–time curve from time zero to infinity, $AUC_{last}$ area under the plasma concentration–time curve from time zero to the time of the last measurable concentration, *CI* confidence interval, *CKD-EPI* Chronic Kidney Disease Epidemiology Collaboration, $C_{max}$ maximum plasma drug concentration, *eGFR* estimated glomerular filtration rate, *PK* pharmacokinetics, $R^2$ regression coefficient.

**a.**



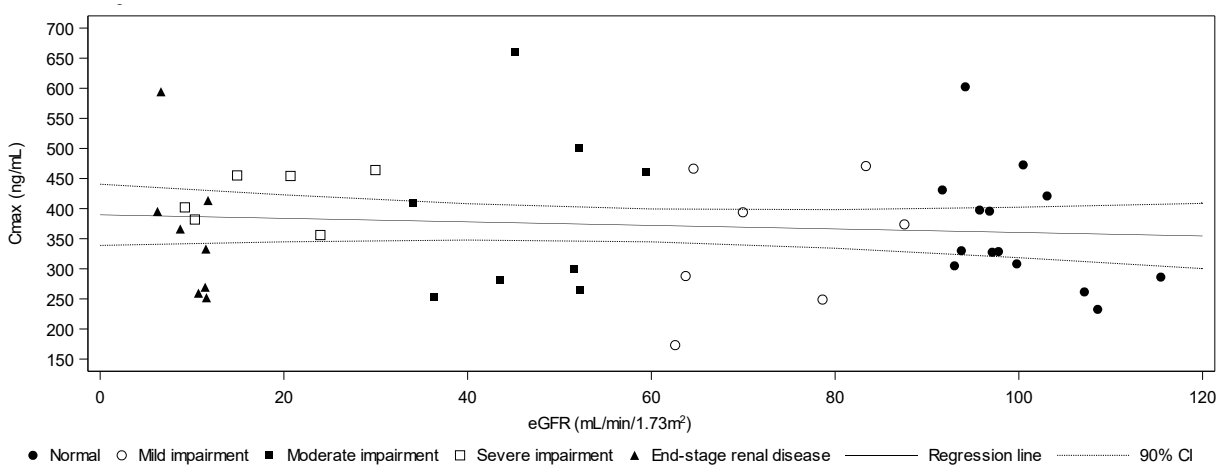

PK = 90167.14 -48.8318*(eGFR); 90% CI and p-value for slope: (-204.6867, 107.0231) [0.6008]; $R^2$ = 0.0067

**b.**




PK = 94578.17 -66.1916*(eGFR); 90% CI and p-value for slope: (-231.3799, 98.9968) [0.5039]; $R^2$ = 0.0110

**c.**

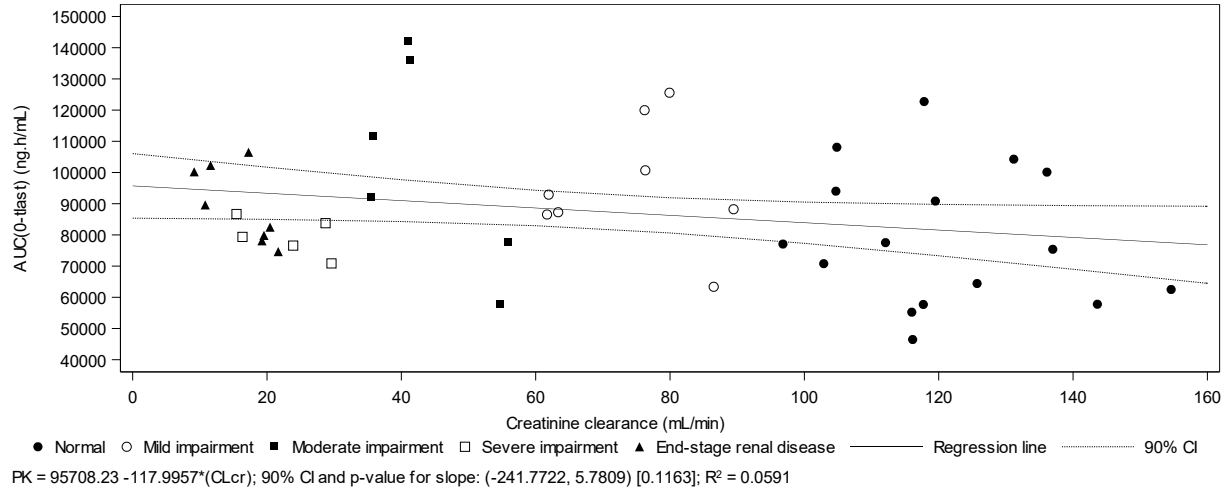



PK = 389.70 -0.2930*(eGFR); 90% CI and p-value for slope: (-1.0411, 0.4551) [0.5135]; $R^2$ = 0.0105

**Supplemental Fig. 2** Relationship between pharmacokinetic parameters of tirzepatide 5 mg and renal function calculated by creatinine clearance (Cockcroft-Gault)

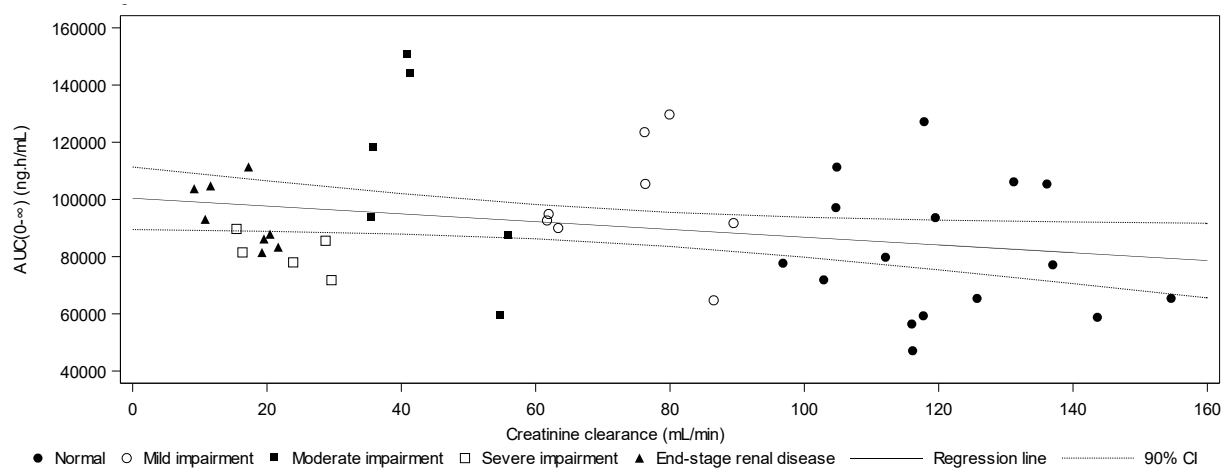
$AUC_{\infty}$ area under the plasma concentration–time curve from time zero to infinity, $AUC_{last}$ area under the plasma concentration–time curve from time zero to the time of the last measurable concentration, *CI* confidence interval, $CL_{CR}$ Creatinine clearance, $C_{max}$ maximum plasma drug concentration, *PK* pharmacokinetics, $R^2$ regression coefficient.

**a.**



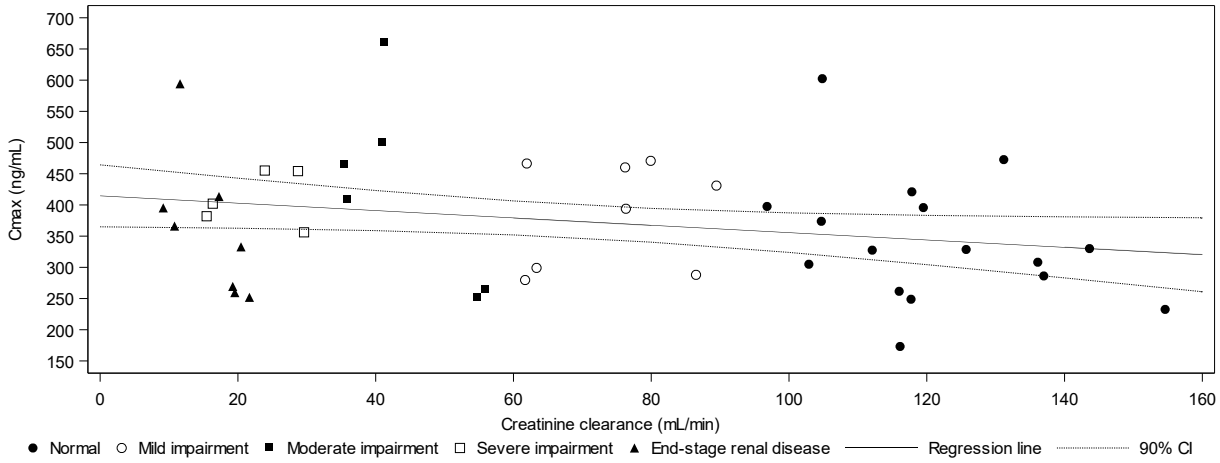

PK = 95708.23 -117.9957*(CLcr); 90% CI and p-value for slope: (-241.7722, 5.7809) [0.1163]; $R^2$ = 0.0591

**b.**




PK = 100402.41 -136.0886*(CLcr); 90% CI and p-value for slope: (-266.8171, -5.3602) [0.0873]; $R^2$ = 0.0696

**c.**




PK = 414.60 -0.5899*(CLcr); 90% CI and p-value for slope: (-1.1837, 0.0038) [0.1021]; $R^2$ = 0.0638