***BMC Pharmacology and Toxicology***

**Additional file 2**

**Pharmacokinetic interactions of esaxerenone with amlodipine and digoxin in healthy Japanese subjects**

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***Supplementary Table S1.*** *Summary of adverse events*

|  |  |  |  |
| --- | --- | --- | --- |
| **Adverse event** | **Study 1** | **Study 2** | **Study 3** |
| **Esaxerenone 2.5 mg** | **Amlodipine 2.5 mg** | **Digoxin 0.25 mg/day** |
| **Alone(n=24)** | **+ Amlodipine****10 mg/day(n=22a)** | **Alone(n=20)** | **+ Esaxerenone****5 mg/day(n=18a)** | **Alone(n=20)** | **+ Esaxerenone 5 mg/day(n=19a)** |
|
| Any TEAE | 1 (4.2) | 1 (4.5) | 1 (5.0) | 0 | 2 (10.0) | 0 |
| Gastroenteritis | 1 (4.2) | 0 | 0 | 0 | 0 | 0 |
| Tonsillitis | 0 | 0 | 1 (5.0) | 0 | 0 | 0 |
| Nasopharyngitis | 0 | 0 | 0 | 0 | 1 (5.0) | 0 |
| Loss of appetite | 1 (4.2) | 0 | 0 | 0 | 0 | 0 |
| Muscle cramp | 0 | 1 (4.5) | 0 | 0 | 0 | 0 |
| Increased alanine aminotransferase  | 0 | 0 | 0 | 0 | 1 (5.0) | 0 |
| Increased aspartate aminotransferase  | 0 | 0 | 0 | 0 | 1 (5.0) | 0 |
| Increased blood creatine phosphokinase | 0 | 1 (4.5) | 0 | 0 | 0 | 0 |

Values are number of subjects (%).

aSubjects who were withdrawn were not included in this analysis.

TEAE, treatment-emergent adverse event.