**Supplemental Digital Content 6.** Results of mixed effect ANOVA for weekly total VAS scores for all gastrointestinal symptoms

Difference of Least Squares Means (Overall and by Lactose Tolerability)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Effect** | **Estimate** | **SE** | **DF** | **t Value** | **Pr > |t|** |
| **Overall** | A2 milk vs. Conventional milk | −1.3205 | 0.0796 | 818 | 16.59 | <0.0001\*\*\* |
|  | Conventional milk | D1 vs. BL | 1.8000 | 0.2070 | 370 | −8.70 | <0.0001\*\*\* |
|  |  | D2 vs. BL | 1.7067 | 0.2070 | 370 | −8.25 | <0.0001\*\*\* |
|  |  | D3 vs. BL | 1.7067 | 0.2070 | 370 | −8.25 | <0.0001\*\*\* |
|  |  | D4 vs. BL | 1.6933 | 0.2070 | 370 | −8.18 | <0.0001\*\*\* |
|  |  | D5 vs. BL | 1.7067 | 0.2070 | 370 | −8.25 | <0.0001\*\*\* |
|  | A2 milk | D1 vs. BL | 0.1467 | 0.1304 | 370 | −1.12 | 0.2614 |
|  |  | D2 vs. BL | 0.2133 | 0.1304 | 370 | −1.64 | 0.1027 |
|  |  | D3 vs. BL | 0.2667 | 0.1304 | 370 | −2.04 | 0.0516 |
|  |  | D4 vs. BL | 0.1733 | 0.1304 | 370 | −1.33 | 0.1846 |
|  |  | D5 vs. BL | 0.1333 | 0.1304 | 370 | −1.02 | 0.3072 |
| **Lactose intolerant** | A2 milk vs. Conventional milk | −1.4397 | 0.0887 | 697 | 16.23 | <0.0001\*\*\* |
| Conventional milk | D1 vs. BL | 1.8438 | 0.2332 | 315 | −7.91 | <0.0001\*\*\* |
|  |  | D2 vs. BL | 1.7813 | 0.2332 | 315 | −7.64 | <0.0001\*\*\* |
|  |  | D3 vs. BL | 1.7969 | 0.2332 | 315 | −7.71 | <0.0001\*\*\* |
|  |  | D4 vs. BL | 1.8750 | 0.2332 | 315 | −8.04 | <0.0001\*\*\* |
|  |  | D5 vs. BL | 1.9062 | 0.2332 | 315 | −8.17 | <0.0001\*\*\* |
|  | A2 milk | D1 vs. BL | 0.0781 | 0.1457 | 315 | −0.54 | 0.5921 |
|  |  | D2 vs. BL | 0.2188 | 0.1457 | 315 | −1.50 | 0.1342 |
|  |  | D3 vs. BL | 0.2656 | 0.1457 | 315 | −1.82 | 0.0692 |
|  |  | D4 vs. BL | 0.2031 | 0.1457 | 315 | −1.39 | 0.1642 |
|  |  | D5 vs. BL | 0.1719 | 0.1457 | 315 | −1.18 | 0.2389 |
| **Lactose tolerant** | A2 milk vs. Conventional milk | −0.6278 | 0.1475 | 114 | 4.26 | <0.0001\*\*\* |
|  | Conventional milk | D1 vs. BL | 1.5455 | 0.3458 | 50 | −4.47 | <0.0001\*\*\* |
|  |  | D2 vs. BL | 1.2727 | 0.3458 | 50 | −3.68 | 0.0006\*\*\* |
|  |  | D3 vs. BL | 1.1818 | 0.3458 | 50 | −3.42 | 0.0013\*\* |
|  |  | D4 vs. BL | 0.6364 | 0.3458 | 50 | −1.84 | 0.0716 |
|  |  | D5 vs. BL | 0.5455 | 0.3578 | 50 | −1.58 | 0.1210 |
|  | A2 milk | D1 vs. BL | 0.5455 | 0.2626 | 50 | −2.01 | 0.0530 |
|  |  | D2 vs. BL | 0.1818 | 0.2626 | 50 | −0.69 | 0.4920 |
|  |  | D3 vs. BL | 0.2727 | 0.2626 | 50 | −1.04 | 0.3041 |
|  |  | D4 vs. BL | −0.0909 | 0.2626 | 50 | 0.00 | 1.0000 |
|  |  | D5 vs. BL | −0.3636 | 0.2626 | 50 | 0.35 | 0.7307 |

The daily total VAS scores for all symptoms were analyzed using a mixed effect ANOVA using fixed effects for study product (conventional milk or milk containing A2 beta-casein only), study phase (1 or 2), and the measurement time in each study phase (denoted as BL, D1, D2, D3, D4, and D5; where BL represent the baseline in phase 1 and 2, and D1-D5 represent the intervention days 1 to 5 in phase 1 and days 15 to 19 in phase 2). A random subject effect was also nested within the sequence of study intervention. A similar analysis was performed when results were stratified by lactose intolerance status. A2 milk = milk containing A2 beta-casein only.

\*: p<0.05; \*\*: p<0.01; \*\*\*: p<0.001; no symbol: p≥≥0.05