## Statistical analysis

**﻿****Sample size determination**

No explicit power analysis was used in this study; sample size was determined on the maximum number of people recruited in research sites.

**Figure2**

Dates are presented as mean ± SEM. Neutralizing antibodies are presented as geometric mean titers (GMT), and their 95% confidence interval (CI) was calculated with Student’s t distribution on log-transformed data and then back-transformed. One-way analysis of variance was used for comparison. Correlations were assessed using Pearson’s correlation coefficient. Two-tailed P values were calculated. ns, not significant, \* P< 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| IgM-S+N | Pre-V | V1-14d | V1-28d | V2-1m | V2-3m | V2-6m | V2-9m | V2-12m |
| Sample number | 91 | 125 | 91 | 100 | 110 | 160 | 190 | 200 |
| Mean | 0.4 | 5.1 | 5.1 | 1.4 | 0.4 | 0.3 | 0.3 | 0.2 |
| Std. Deviation | 0.2 | 11.7 | 9.1 | 2.4 | 0.7 | 0.5 | 0.5 | 0.4 |
| Std. Error of Mean | 0.0 | 1.1 | 0.9 | 0.2 | 0.1 | 0.04 | 0.04 | 0.03 |
| positive number | 3 | 72 | 69 | 33 | 4 | 7 | 9 | 4 |
| positive rate% | 3.3 | 57.6 | 75.8 | 33.0 | 3.6 | 4.4 | 4.7 | 2.0 |
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| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V1-14d | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V1-28d | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-1m | No | ns | 0.8517 |
| Pre-V vs. V2-3m | No | ns | >0.9999 |
| Pre-V vs. V2-6m | No | ns | >0.9999 |
| Pre-V vs. V2-9m | No | ns | >0.9999 |
| Pre-V vs. V2-12m | No | ns | >0.9999 |
| V1-14d vs. V1-28d | No | ns | >0.9999 |
| V1-14d vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| V1-14d vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V1-14d vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V1-14d vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V1-14d vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-3m | No | ns | 0.8149 |
| V2-1m vs. V2-6m | No | ns | 0.6564 |
| V2-1m vs. V2-9m | No | ns | 0.6368 |
| V2-1m vs. V2-12m | No | ns | 0.4681 |
| V2-3m vs. V2-6m | No | ns | >0.9999 |
| V2-3m vs. V2-9m | No | ns | >0.9999 |
| V2-3m vs. V2-12m | No | ns | >0.9999 |
| V2-6m vs. V2-9m | No | ns | >0.9999 |
| V2-6m vs. V2-12m | No | ns | >0.9999 |
| V2-9m vs. V2-12m | No | ns | >0.9999 |
|  |  |  |  |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| IgG-S+N | Pre-V | V1-14d | V1-28d | V2-1m | V2-3m | V2-6m | V2-9m | V2-12m |
| Sample number | 91 | 125 | 91 | 100 | 110 | 160 | 190 | 200 |
| Mean | 0.6 | 3.7 | 64.3 | 79.7 | 29.4 | 10.5 | 8.9 | 6.8 |
| Std. Deviation | 0.6 | 5.6 | 55.3 | 57.1 | 24.8 | 11.3 | 14.1 | 13.1 |
| Std. Error of Mean | 0.1 | 0.5 | 5.8 | 5.7 | 2.4 | 0.9 | 1.0 | 0.9 |
| positive number | 0 | 9 | 89 | 97 | 97 | 52 | 42 | 27 |
| positive rate% | 0.0 | 7.2 | 97.8 | 97.0 | 88.2 | 32.5 | 22.1 | 13.5 |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V1-14d | No | ns | 0.9912 |
| Pre-V vs. V1-28d | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-6m | No | ns | 0.0936 |
| Pre-V vs. V2-9m | No | ns | 0.2236 |
| Pre-V vs. V2-12m | No | ns | 0.5955 |
| V1-14d vs. V1-28d | Yes | \*\*\*\* | <0.0001 |
| V1-14d vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| V1-14d vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V1-14d vs. V2-6m | No | ns | 0.3971 |
| V1-14d vs. V2-9m | No | ns | 0.6856 |
| V1-14d vs. V2-12m | No | ns | 0.9701 |
| V1-28d vs. V2-1m | Yes | \*\* | 0.0020 |
| V1-28d vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V1-28d vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V2-6m vs. V2-9m | No | ns | 0.9994 |
| V2-6m vs. V2-12m | No | ns | 0.9028 |
| V2-9m vs. V2-12m | No | ns | 0.9942 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| IgM-RBD | Pre-V | V2-1m | V2-3m | V2-6m | V2-9m | V2-12m |
| Sample number |  | 100 | 110 | 160 | 190 | 200 |
| Mean | 0.1 | 1.8 | 0.5 | 0.6 | 0.7 | 0.1 |
| Std. Deviation | 0.1 | 4.5 | 0.4 | 0.7 | 1.0 | 0.3 |
| Std. Error of Mean | 0.01 | 0.4 | 0.04 | 0.1 | 0.1 | 0.02 |
| positive number | 0 | 38.0 | 10.0 | 34.0 | 65.0 | 3.0 |
| positive rate% |  | 38.0 | 9.1 | 21.3 | 34.2 | 1.5 |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-3m | No | ns | 0.5111 |
| Pre-V vs. V2-6m | No | ns | 0.2120 |
| Pre-V vs. V2-9m | No | ns | 0.0711 |
| Pre-V vs. V2-12m | No | ns | 0.9997 |
| V2-1m vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-6m | No | ns | 0.9977 |
| V2-3m vs. V2-9m | No | ns | 0.9411 |
| V2-3m vs. V2-12m | No | ns | 0.4531 |
| V2-6m vs. V2-9m | No | ns | 0.9958 |
| V2-6m vs. V2-12m | No | ns | 0.1078 |
| V2-9m vs. V2-12m | Yes | \* | 0.0166 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| IgG-RBD | Pre-V | V2-1m | V2-3m | V2-6m | V2-9m | V2-12m |
| Sample number |  | 100 | 110 | 160 | 190 | 200 |
| Mean | 0.04 | 18.0 | 5.6 | 2.3 | 2.1 | 1.9 |
| Std. Deviation | 0.08 | 16.3 | 4.8 | 2.0 | 3.2 | 3.9 |
| Std. Error of Mean | 0.01 | 1.6 | 0.5 | 0.2 | 0.2 | 0.3 |
| positive number | 0.00 | 97.0 | 110.0 | 121.0 | 119.0 | 93.0 |
| positive rate% |  | 97.0 | 100.0 | 75.6 | 62.6 | 46.5 |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-6m | No | ns | 0.1086 |
| Pre-V vs. V2-9m | No | ns | 0.1748 |
| Pre-V vs. V2-12m | No | ns | 0.2370 |
| V2-1m vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-6m | Yes | \*\*\* | 0.0006 |
| V2-3m vs. V2-9m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-12m | Yes | \*\*\*\* | <0.0001 |
| V2-6m vs. V2-9m | No | ns | 0.9993 |
| V2-6m vs. V2-12m | No | ns | 0.9935 |
| V2-9m vs. V2-12m | No | ns | >0.9999 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| pseudovirus | Pre-V | V2-1m | V2-3m | V2-6m | V2-9m | V2-12m |
| Sample number |  | 100 | 110 | 160 | 190 | 200 |
| Mean | 3.2 | 76.2 | 55.7 | 37.5 | 26.6 | 24.0 |
| Std. Deviation | 6.2 | 16.2 | 17.3 | 18.8 | 18.5 | 21.7 |
| Std. Error of Mean | 0.7 | 1.6 | 1.7 | 1.5 | 1.3 | 1.5 |
| positive number | 0.00 | 92.0 | 68.0 | 40.0 | 22.0 | 23.0 |
| positive rate% |  | 92.0 | 61.8 | 25.0 | 11.6 | 11.5 |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-6m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-9m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-1m vs. V-3m | Yes | \*\*\*\* | <0.0001 |
| V-1m vs. V-6m | Yes | \*\*\*\* | <0.0001 |
| V-1m vs. V-9m | Yes | \*\*\*\* | <0.0001 |
| V-1m vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-3m vs. V-6m | Yes | \*\*\*\* | <0.0001 |
| V-3m vs. V-9m | Yes | \*\*\*\* | <0.0001 |
| V-3m vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-6m vs. V-9m | Yes | \*\*\*\* | <0.0001 |
| V-6m vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-9m vs. V-12m | No | ns | 0.7256 |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Neutralizing antibody  | Pre-V | V2-1m | V2-3m | V2-6m | V2-9m | V2-12m |
| Sample number |  | 100 | 110 | 160 | 190 | 200 |
| GMT | 2.2 | 20.2 | 14.7 | 7.8 | 6.0 | 4.1 |
| Lower 95% CI of geo. mean | 2.1 | 16.3 | 12.7 | 6.9 | 5.3 | 3.7 |
| Upper 95% CI of geo. mean | 2.3 | 24.9 | 17.0 | 8.8 | 6.7 | 4.5 |
| 25% Percentile | 2 | 12 | 8 | 6 | 4 | 2 |
| 75% Percentile | 2 | 32 | 24 | 15 | 8 | 6 |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-6m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-9m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-1m vs. V-3m | No | ns | 0.1872 |
| V-1m vs. V-6m | Yes | \*\*\*\* | <0.0001 |
| V-1m vs. V-9m | Yes | \*\*\*\* | <0.0001 |
| V-1m vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-3m vs. V-6m | Yes | \*\*\*\* | <0.0001 |
| V-3m vs. V-9m | Yes | \*\*\*\* | <0.0001 |
| V-3m vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-6m vs. V-9m | Yes | \* | 0.0239 |
| V-6m vs. V-12m | Yes | \*\*\*\* | <0.0001 |
| V-9m vs. V-12m | Yes | \*\*\*\* | <0.0001 |

**Figure3**

Dates are presented as mean ± SEM. Neutralizing antibodies are presented as geometric mean titers (GMT), and their 95% confidence interval (CI) was calculated with Student’s t distribution on log-transformed data and then back-transformed. One-way analysis of variance was used for comparison. Correlations were assessed using Pearson’s correlation coefficient. Two-tailed P values were calculated. ns, not significant, \* P< 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| IgG-RBD | V2-1m | V2-3m | V2-6m | V3-1m |
| Sample number | 90.0  | 90.0  | 90.0  | 90.0  |
| Mean | 9.4  | 2.8  | 2.8  | 21.7  |
| Std. Deviation | 7.9  | 3.0  | 2.4  | 16.8  |
| Std. Error of Mean | 0.8  | 0.3  | 0.2  | 1.8  |
| positive number | 90.0  | 74.0  | 78.0  | 89.0  |
| positive rate% | 100.0  | 82.2  | 86.7  | 98.9  |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-6m | No | ns | >0.9999 |
| V2-3m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-6m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| IgG-S+N | V2-1m | V2-3m | V2-6m | V3-1m |
| Sample number | 90.0  | 90.0  | 90.0  | 90.0  |
| Mean | 67.4  | 24.3  | 9.4  | 131.3  |
| Std. Deviation | 47.2  | 23.0  | 15.1  | 81.1  |
| Std. Error of Mean | 5.0  | 2.5  | 1.6  | 8.6  |
| positive number | 87.0  | 66.0  | 28.0  | 89.0  |
| positive rate% | 96.7  | 73.3  | 31.1  | 98.9  |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-6m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Neutralizing antibody | Pre-V | V2-1m | V2-3m | V2-6m | V3-1m |
| Sample number | 90.0  | 89.0  | 88.0  | 90.0  | 90.0  |
| Geometric mean | 2.1  | 29.4  | 15.5  | 6.6  | 168.2  |
| Geometric SD factor | 1.3  | 2.1  | 2.1  | 2.6  | 2.4  |
| Lower 95% CI of geo. mean | 2.0  | 25.3  | 13.3  | 5.4  | 139.7  |
| Upper 95% CI of geo. mean | 2.2  | 34.2  | 18.0  | 8.0  | 202.6  |
| positive number | 3.0  | 88.0  | 84.0  | 52.0  | 90.0  |
| positive rate% | 3.3  | 98.9  | 95.5  | 57.8  | 100.0  |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-6m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| pseudovirus | Pre-V | V2-1m | V2-3m | V2-6m | V3-1m |
| Sample number | 90.0  | 89.0  | 88.0  | 89.0  | 90.0  |
| Mean | 8.6  | 72.7  | 44.1  | 21.4  | 84.3  |
| Std. Deviation | 9.4  | 14.7  | 16.6  | 16.4  | 16.2  |
| Std. Error of Mean | 1.0  | 1.6  | 1.8  | 1.7  | 1.7  |
| positive number | 0.0  | 80.0  | 33.0  | 6.0  | 86.0  |
| positive rate% | 0.0  | 89.9  | 37.5  | 6.7  | 95.6  |

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| Pre-V vs. V2-1m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| Pre-V vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-3m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-1m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V2-6m | Yes | \*\*\*\* | <0.0001 |
| V2-3m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |
| V2-6m vs. V3-1m | Yes | \*\*\*\* | <0.0001 |

**Figure4**

Dates are presented as mean ± SEM. Neutralizing antibodies are presented as geometric mean titers (GMT), and their 95% confidence interval (CI) was calculated with Student’s t distribution on log-transformed data and then back-transformed. The paired Student's t-test and one-way analysis of variance were used for comparison. Two-tailed P values were calculated. ns, not significant, \* P< 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

**V2-1m**

|  |  |  |  |
| --- | --- | --- | --- |
| Multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| WT vs. Delta | Yes | \*\*\*\* | <0.0001 |
| WT vs. Omicron | Yes | \*\*\*\* | <0.0001 |
| Delta vs. Omicron | Yes | \*\*\*\* | <0.0001 |

**V3-1m**

|  |  |  |  |
| --- | --- | --- | --- |
| Tukey's multiple comparisons test | Below threshold? | Summary | Adjusted P Value |
| WT vs. Delta | Yes | \*\*\*\* | <0.0001 |
| WT vs. Omicron | Yes | \*\*\*\* | <0.0001 |
| Delta vs. Omicron | Yes | \*\*\*\* | <0.0001 |

**Delta**

|  |  |
| --- | --- |
| Paired t test |  |
| P value | 0.0268 |
| P value summary | \* |
| Significantly different (P < 0.05)? | Yes |
| One- or two-tailed P value? | Two-tailed |
| t, df | t=2.253, df=88 |
| Number of pairs | 89 |

**Omicron**

|  |  |
| --- | --- |
| Paired t test |  |
| P value | 0.0035 |
| P value summary | \*\* |
| Significantly different (P < 0.05)? | Yes |
| One- or two-tailed P value? | Two-tailed |
| t, df | t=3.002, df=88 |
| Number of pairs | 89 |