**Supplementary Tables**

Table S1. CD8+ T lymphocyte quantification

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **CD8+ T lymphocyte measurement** | **Mean** | **SD** | **Median** | **Min** | **Max** | **N** |
| **Overall population** | |  |  |  |  |  |
| Pretreatment, intratumoral | 1376.26 | 1164.40 | 1065 | 54.0 | 4362 | 27 |
| Pretreatment, leading edge | 1960.74 | 1145.95 | 1965 | 20.0 | 4714 | 27 |
| Posttreatment, intratumoral  **Per treatment arm (ratio)**  Posttreatment/pretreatment, durvalumab  Posttreatment/pretreatment, durvalumab + tremelimumab | 2091.79  3.88  6.05 | 1743.51  7.18  14.63 | 1829.0  1.31  1.15 | 140.0  0.07  0.39 | 6973  26.15  50.04 | 24  12  11 |

NOTE: Data are provided as cells/mm2 unless otherwise indicated.

Abbreviations: SD, standard deviation; Max, maximum; Min, minimum.

Table S2. Antitumor activity by treatment arm

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Response | Total (No,%) | Durva (No, %) | Durva+Treme (No, %) | P-value |
| Response RECIST (N=28)\* |  |  |  |  |
| PR | 12 (42.86) | 6 (42.86) | 6 (42.86) | >0.99 |
| SD | 14 (50) | 8 (57.14) | 6 (42.86) |  |
| PD | 2 (7.14) | 0 (0) | 2 (14.29) |  |
| Pathologic response (N=25)\*\* |  |  |  |  |
| <=10% viable tumor cells | 2 (8) | 1 (7.69) | 1 (8.33) | >0.99 |
| 11%-50% viable tumor cells | 11 (44) | 5 (38.46) | 6 (50) | 0.695 |
| 51%-89% viable tumor cells | 6 (24) | 4 (30.77) | 2 (16.67) | >0.99 |
| >=90% viable tumor cells | 6 (24) | 3 (23.08) | 3 (25) |  |

Abbreviations: durva, durvalumab; PD, progressive disease; PR, partial response; SD, stable disease; treme, tremelimumab.

*\* Response is defined as complete or partial response. There were no complete responses. The p-value compares PR vs. SD+PD between treatment groups.*

*\*\* The p-values shown compare the percentage of tumor cells in that group or lower versus a greater percentage of viable tumor cells, between treatment groups.*

Table S3. Association between pathologic response and response by imaging (RECIST) (N=25)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Pathologic response**  **(primary tumor site)** | **Viable tumor cells, %** | **PR, No. (%)** | **SD, No. (%)** | **P value\*** |
| Treatment effect |  |  |  |  |
| Yes | <90 | 12 (100) | 7 (54) | 0.015 |
| No | ≥90 | 0 (0) | 6 (46) |  |
| Partial pathologic response |  |  |  |  |
| Yes | ≤50 | 10 (83) | 3 (23) | 0.005 |
| No | >50 | 2 (17) | 10 (77) |  |

\*Two-sided Fisher’s exact test.

Abbreviations: PR, partial response; SD, stable disease.

Table S4. Association between response by imaging (RECIST) and pathologic response by site (primary vs. node)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | Response RECIST | Mean | Std. dev. | Median | Min | Max | N | P value\* |
| Viable tumor cells, primary tumor, % | PR | 34.08 | 23.12 | 37.5 | 0 | 70 | 12 | <0.001 |
|  | SD | 74.23 | 22.44 | 80 | 20 | 95 | 13 |  |
| Viable tumor cells, nodes, % | PR | 39.5 | 38.9 | 35 | 0 | 90 | 8 | 0.602 |
|  | SD | 52.27 | 40.95 | 75 | 0 | 90 | 11 |  |

\*Two-sided Wilcoxon rank-sum test.

Abbreviations: PR, partial response; SD, stable disease; Std. dev., standard deviation; Max, maximum; Min, minimum.

*Table S5. Patterns of MDASI-HN assessments*

|  |  |
| --- | --- |
| **MDASI-HN(s) completed** | **No. of patients\*** |
| Day 1, day 29, and pre-surgery | 14 |
| Day 1 and day 29 only | 6 |
| Day 1 and pre-surgery only | 2 |
| Day 29 and pre-surgery only | 1 |
| Day 1 only | 1 |

Abbreviation: MDASI-HN, MD Anderson Symptom Inventory Head and Neck Module.

\*Twenty-two patients completed MDASIs on day 1, 21 completed MDASIs on day 29, and 18 completed MDASIs pre-surgery; thus, 61 completed MDASIs were available for analysis.

*Table S6. Median global MDASI scores*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Time Point | Total | | | | |  | Durva | | | | |  | Durva + Treme | | | | |
| *n* | Median | Min | Max | IQR |  | *n* | Median | Min | Max | IQR |  | *n* | Median | Min | Max | IQR |
| Day 1 | 22 | 0.49 | 0.00 | 4.18 | 0.77 |  | 11 | 0.23 | 0.00 | 4.18 | 1.09 |  | 11 | 0.88 | 0.00 | 2.86 | 0.64 |
| Day 29 | 21 | 0.41 | 0.00 | 3.23 | 1.41 |  | 9 | 0.32 | 0.09 | 3.23 | 0.55 |  | 12 | 0.57 | 0.00 | 2.95 | 1.74 |
| Pre-surgery | 18 | 0.56 | 0.05 | 3.77 | 1.27 |  | 9 | 0.32 | 0.05 | 3.77 | 1.27 |  | 9 | 0.57 | 0.09 | 3.52 | 0.49 |

Abbreviations: durva, durvalumab; IQR, interquartile range; MDASI-HN, MD Anderson Symptom Inventory Head and Neck Module; Max, maximum; Min, minimum; treme, tremelimumab.

*Table S7. Differences of least squares means for durva vs. durva + treme with Tukey-Kramer adjustment, effect arm\*timept, alpha = .05*

| MDASI time point | Estimate | Standard error | DF | t Value | Pr > |t| | Adj P | Lower | Upper | Adj lower | Adj upper |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Day 1 | -0.5214 | 0.5988 | 33 | -0.87 | 0.3902 | 0.9509 | -1.7396 | 0.6968 | -2.3317 | 1.2890 |
| Day 29 | -0.2265 | 0.6173 | 33 | -0.37 | 0.7160 | 0.9990 | -1.4823 | 1.0293 | -2.0928 | 1.6398 |
| Pre-surgery | -0.1011 | 0.6553 | 33 | -0.15 | 0.8784 | 1.0000 | -1.4344 | 1.2322 | -2.0825 | 1.8803 |

Abbreviations: adj, adjusted; durva, durvalumab; MDASI-HN, MD Anderson Symptom Inventory Head and Neck Module; treme, tremelimumab.

*Table S8. Differences of least squares means across time points within treatment arm with Tukey-Kramer Adjustment, Effect arm\*timept, Alpha = .05*

| Treatment | MDASI time point | MDASI time point | Estimate | Standard error | DF | t Value | Pr > |t| | Adj P | Lower | Upper | Adj lower | Adj upper |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Durva | Day 1 | Day 29 | -0.3844 | 0.5479 | 33 | -0.70 | 0.4878 | 0.9804 | -1.4992 | 0.7304 | -2.0411 | 1.2722 |
| Durva | Day 1 | Pre-surgery | -0.6703 | 0.5551 | 33 | -1.21 | 0.2358 | 0.8300 | -1.7998 | 0.4591 | -2.3488 | 1.0081 |
| Durva | Day 29 | Pre-surgery | -0.2859 | 0.5908 | 33 | -0.48 | 0.6316 | 0.9964 | -1.4879 | 0.9161 | -2.0722 | 1.5004 |
| Durva + treme | Day 1 | Day 29 | -0.08955 | 0.5058 | 33 | -0.18 | 0.8606 | 1.0000 | -1.1186 | 0.9395 | -1.6188 | 1.4397 |
| Durva+ treme | Day 1 | Pre-surgery | -0.2500 | 0.5538 | 33 | -0.45 | 0.6546 | 0.9974 | -1.3768 | 0.8767 | -1.9245 | 1.4245 |
| Durva+ treme | Day 29 | Pre-surgery | -0.1605 | 0.5399 | 33 | -0.30 | 0.7681 | 0.9997 | -1.2589 | 0.9379 | -1.7928 | 1.4719 |

Abbreviations: adj, adjusted; durva, durvalumab; MDASI-HN, MD Anderson Symptom Inventory Head and Neck Module; treme, tremelimumab.