**Supplemental Table 2:** *TP53* mutations scored and stratified by EAp53 in the training dataset with associated demographic data.

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| **Training Set** |
| **Mutation** | **EA Score** | **EA Risk** | **Age** | **Primary Tumor Site** | **T Stage** | **N Stage** |
| p.S106R | 21.82 | Low | 77 | Larynx | T2 | N0 |
| p.E224D | 39.02 | Low | 65 | Oral Tongue | T2 | N0 |
| p.V143M | 51.72 | Low | 72 | Buccal Mucosa | T4a | N0 |
| p.V143M | 51.72 | Low | 77 | Oral Tongue | NA | NA |
| p.V157F | 55.26 | Low | 64 | Larynx | T4a | N2c |
| p.R158L | 57.61 | Low | 68 | Larynx | T4a | N2c |
| p.E258D | 57.73 | Low | 69 | Oral Tongue | T3 | N2c |
| p.R337L | 61.55 | Low | 53 | Larynx | T2 | N0 |
| p.A159V | 62.4 | Low | 65 | Oral Cavity | T2 | N0 |
| p.H168L | 62.62 | Low | 19 | Oral Tongue | T2 | N0 |
| p.Y236C | 62.93 | Low | 65 | Larynx | T3 | N0 |
| p.Y234C | 62.94 | Low | 57 | Oral Tongue | T4a | N2c |
| p.V272M | 63.49 | Low | 79 | Oral Tongue | T2 | N0 |
| p.R337C | 63.66 | Low | 71 | Larynx | T4a | N0 |
| p.M237I | 63.68 | Low | 79 | Oral Cavity | NA | NA |
| p.P151S | 64.12 | Low | 87 | Floor of Mouth | NA | NA |
| p.L137Q | 64.66 | Low | 66 | Buccal Mucosa | T2 | N1 |
| p.V172F | 65.55 | Low | 53 | Larynx | T4a | N3 |
| p.R273H | 66.12 | Low | 61 | Oral Tongue | T1 | N0 |
| p.R273H | 66.12 | Low | 46 | Oral Tongue | T3 | N1 |
| p.R273H | 66.12 | Low | 62 | Oral Tongue | T3 | N0 |
| p.R273H | 66.12 | Low | 39 | Oral Cavity | NA | NA |
| p.R273H | 66.12 | Low | 69 | Oral Tongue | T2 | N0 |
| p.R273H | 66.12 | Low | 67 | Larynx | T2 | N0 |
| p.R273H | 66.12 | Low | 70 | Oral Tongue | T3 | N2c |
| p.E285K | 69.87 | Low | 85 | Oral Cavity | T2 | N0 |
| p.E285K | 69.87 | Low | 78 | Oral Cavity | T3 | N1 |
| p.Y163C | 70 | Low | 74 | Larynx | T4a | N2 |
| p.P151T | 70.26 | Low | 51 | Hypopharynx | T4a | N2c |
| p.Q136P | 71.29 | Low | 39 | Larynx | T3 | N2c |
| p.P151H | 71.97 | Low | 53 | Oral Tongue | T4a | N0 |
| p.I195T | 72.13 | Low | 70 | Oral Tongue | T2 | N0 |
| p.Y220C | 72.52 | Low | 57 | Oral Cavity | T4a | N1 |
| p.R282W | 73.21 | Low | 62 | Oral Tongue | T3 | N0 |
| p.R282W | 73.21 | Low | 56 | Oral Cavity | NA | NA |
| p.R282W | 73.21 | Low | 62 | Larynx | T3 | N0 |
| p.R282W | 73.21 | Low | 58 | Oral Cavity | T3 | N0 |
| p.V216M | 73.3 | Low | 60 | Oral Cavity | T4a | N2b |
| p.E271V | 74.39 | Low | 67 | Larynx | T4a | N2a |
| p.F270C, p.T211I | 66.32, 68.48 | Low | 67 | Floor of Mouth | T3 | N0 |
| p.Y220C, p.R110L | 72.52, 28.14 | Low | 57 | Oral Tongue | T4a | N2b |
| p.139\_142KTCP>T, p.M1V | 43.89 | Low | 49 | Oropharynx | T3 | N0 |
| p.S166\*, p.R158H | 43.94 | Low | 87 | Buccal Mucosa | T4b | N2b |
| p.Y236C, p.R213\* | 62.93 | Low | 60 | Larynx | T4a | N1 |
| p.R282W, p.P89fs | 73.21, | Low | 61 | Larynx | T4a | N2b |
| p.V173M | 75.53 | High | 63 | Oral Cavity | T4a | N1 |
| p.V173M | 75.53 | High | 60 | Larynx | T3 | N0 |
| p.E286K | 76.21 | High | 62 | Oropharynx | T2 | N0 |
| p.H179Y | 77.78 | High | 62 | Larynx | T4a | N0 |
| p.Y205C | 77.88 | High | 66 | Oral Tongue | T3 | N2b |
| p.R175H | 78.51 | High | 52 | Oral Tongue | T2 | N0 |
| p.R175H | 78.51 | High | 47 | Floor of Mouth | NA | NA |
| p.R175H | 78.51 | High | 45 | Larynx | T3 | N0 |
| p.R175H | 78.51 | High | 76 | Larynx | T4a | N0 |
| p.R248Q | 78.95 | High | 59 | Oral Tongue | T4a | N2b |
| p.R248Q | 78.95 | High | 26 | Oral Tongue | NA | NA |
| p.R248Q | 78.95 | High | 54 | Oral Cavity | T4a | N0 |
| p.R248Q | 78.95 | High | 29 | Oral Tongue | NA | NA |
| p.L194P | 79.72 | High | 53 | Larynx | NA | NA |
| p.Y126C | 81.09 | High | 64 | Oral Cavity | T2 | NX |
| p.H179R | 81.91 | High | 66 | Tonsil | T3 | N2c |
| p.V173L | 82.64 | High | 68 | Floor of Mouth | T4a | N2b |
| p.R248W | 84.11 | High | 85 | Oral Cavity | T4a | N2c |
| p.R248W | 84.11 | High | 74 | Base of Tongue | T3 | N0 |
| p.R248W | 84.11 | High | 48 | Oral Tongue | NA | NA |
| p.R248W | 84.11 | High | 82 | Oral Cavity | T2 | N0 |
| p.R248W | 84.11 | High | 45 | Oral Tongue | T2 | N0 |
| p.L265R | 84.18 | High | 66 | Oral Tongue | T4a | N2 |
| p.P278S | 84.34 | High | 55 | Larynx | T2 | N1 |
| p.R273C | 84.52 | High | 70 | Larynx | T2 | N2 |
| p.H193R | 85.96 | High | 54 | Larynx | T2 | N2c |
| p.G245S | 86.45 | High | 56 | Alveolar Ridge | T4a | N0 |
| p.G245S | 86.45 | High | 64 | Floor of Mouth | T4a | N1 |
| p.G245S | 86.45 | High | 73 | Larynx | NA | NA |
| p.C238S | 86.53 | High | 72 | Larynx | T2 | N0 |
| p.C242S | 86.74 | High | 67 | Larynx | T3 | N0 |
| p.C176S | 86.9 | High | 58 | Oral Tongue | NA | NA |
| p.G262V | 88.02 | High | 69 | Lip | T1 | N1 |
| p.S127F | 88.07 | High | 59 | Larynx | T3 | N0 |
| p.R267P | 88.48 | High | 68 | Larynx | T3 | N0 |
| p.G105C | 90.8 | High | 74 | Oral Cavity | T2 | N0 |
| p.G266R | 91.41 | High | 69 | Oral Tongue | T3 | N1 |
| p.K132N | 92.16 | High | 61 | Larynx | T4a | N1 |
| p.Y236D | 92.17 | High | 50 | Oral Tongue | T3 | N1 |
| p.G266E | 93.08 | High | 76 | Floor of Mouth | T3 | N1 |
| p.E258A | 93.29 | High | 55 | Oral Cavity | T2 | N0 |
| p.C242Y | 93.46 | High | 60 | Larynx | NA | NA |
| p.V173G | 93.47 | High | 64 | Larynx | T4a | N2 |
| p.M133K | 93.62 | High | 60 | Larynx | T3 | N0 |
| p.R249S | 93.65 | High | 60 | Larynx | T4a | NX |
| p.Y126S | 94.81 | High | 66 | Larynx | T3 | N1 |
| p.H193L | 95.4 | High | 38 | Tonsil | NA | NA |
| p.H193L | 95.4 | High | 41 | Oral Tongue | T4a | N2b |
| p.R196P | 95.55 | High | 47 | Floor of Mouth | T4a | N2c |
| p.R280G | 95.71 | High | 69 | Buccal Mucosa | T2 | N1 |
| p.C242F | 97.04 | High | 67 | Larynx | T4a | N0 |
| p.C242F | 97.04 | High | 63 | Larynx | T4a | N2b |
| p.C275F | 97.06 | High | 60 | Oral Tongue | NA | NA |
| p.C275F | 97.06 | High | 65 | Oral Tongue | T3 | N0 |
| p.G245V | 98.74 | High | 55 | Floor of Mouth | T2 | N0 |
| p.G245V | 98.74 | High | 51 | Larynx | T3 | N2a |
| p.H179P | 98.89 | High | 40 | Oral Tongue | T2 | N0 |
| p.R282W, p.R175H | 73.21, 78.51 | High | 67 | Oral Cavity | T4a | N2b |
| p.R283P, p.R175H | 75.75, 78.51 | High | 65 | Hard Palate | T4a | N1 |
| p.M237V, p.H179R | 75.79, 81.91 | High | 60 | Floor of Mouth | T4a | NX |
| p.R248Q, p.G245S | 78.95, 86.45 | High | 64 | Larynx | T4a | N0 |
| p.H179R, p.V157F | 81.91, 55.26 | High | 73 | Oral Cavity | NA | NA |
| p.P278S, p.R213L | 84.34, 90.71 | High | 60 | Larynx | T4a | N2c |
| p.R273C, p.A161T | 84.52, 58.51 | High | 60 | Oral Tongue | T4a | N0 |
| p.G262V, p.Q136H | 88.02, 47.50 | High | 78 | Oral Cavity | T4a | N2b |
| p.Q331H, p.R249M, p.G245D | 9.79, 95.41, 89.56 | High | 61 | Larynx | T4a | N1 |
| p.H193P, p.H179Y | 92.46, 77.78 | High | 73 | Larynx | T3 | N2 |
| p.C176Y, p.R110L | 93.11, 28.14 | High | 64 | Oral Cavity | T4a | N1 |
| p.C238F, p.R156P | 96.54, 42.93 | High | 62 | Larynx | T3 | N0 |
| p.Q331\*, p.H179Y | 77.78 | High | 53 | Larynx | NA | NA |
| p.R175H, p.Y126\_splice | 78.51, | High | 78 | Oral Tongue | NA | NA |
| p.S261\_splice, p.R248W | 84.11 | High | 49 | Larynx | T4a | N1 |
| p.P278S, p.Y205fs | 84.34 | High | 57 | Alveolar Ridge | T4a | N0 |
| p.E336\*, p.G245S | 86.45 | High | 52 | Oral Tongue | T3 | N2b |
| p.C229fs, p.S127Y | 87.62 | High | 69 | Oral Tongue | T3 | N2b |
| p.V218G, p.L194fs | 89.92 | High | 52 | Floor of Mouth | T3 | N0 |
| p.G266E, p.E56\* | 93.08 | High | 65 | Floor of Mouth | T3 | N2b |
| p.R249S, p.L32\_splice | 93.65 | High | 67 | Alveolar Ridge | T4a | N2b |
| p.E286V, p.P58fs | 94.09 | High | 47 | Larynx | NA | NA |
| p.R280S, p.L32\_splice | 94.74 | High | 83 | Oral Cavity | T2 | N0 |
| p.H193L, p.PHHERC177del | 95.4 | High | 28 | Oral Tongue | T2 | N2b |
| p.A307\_splice, p.R280T | 96.08 | High | 73 | Hard Palate | T4a | N0 |