**Supplementary Table 1.** ICI-Related Phase III RCTs in Previously Untreated Advanced NSCLC without Driver Mutations

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Keynote-024** | **Keynote-189** | **Keynote-407** | **Checkmate-277** | **Checkmate-9LA** |
| **PD-L1 Status** | ≥50% | All comers | All comers | All comers | All comers |
| PD-L1≥1% | PD-L1<1% |
| **Randomization Arms** | P | C | P+C | C | P+C | C | N+I | N | C | N+I | N+C | C | N+I+C | C |
| **Age****(median)** | 65 | 66 | 65 | 64 | 65 | 65 | 64 | 64 | 64 | 63 | 64 | 64 | 65 | 65 |
| **Total N** | 154 | 151 | 410 | 206 | 278 | 281 | 396 | 396 | 397 | 187 | 177 | 186 | 361 | 358 |
| **ECOG**012 | 35%64%0% | 35%65%0% | 45%55%0% | 39%61%0% | 26%74%0% | 32%68%0% | 34%66%0% | 36%64%0% | 34%65%1% | 37%62%1% | 33%66%1% | 31%68%1% | 31%68%0% | 31%68%0% |
| **Histology**SquamNon-Squam | 19%81% | 18%82% | N/A100% | N/A100% | 100%N/A | 100%N/A | 30%70% | 30%70% | 29%71% | 25%75% | 24%76% | 25%75% | 31%69% | 31%69% |
| **Brain Metastasis** | 12% | 7% | 18% | 7% | 7% | 9% | 10% | 11% | 10% | 12% | 9% | 6% | 18% | 16% |
| **Follow-Up Duration****(median)** | 5-Year Update59.9 months  | Updated Analysis23.1 months | 3-Year Update40.1 months | 4-Year UpdateMinimum 49.4 months | Minimum 8.1 months |
| **Median Duration of Treatment (months)** | 7.9  | 3.5  | 9.8  | 6.2  | NR | NR | 4.2  | 4.6  | 2.7  | 4.0  | 5.8  | 2.6  | 6.1  | 2.4  |
| **OS**ITTMedian(months)HR (95%CI)PD-L1 Status*≥50%*Median (months)HR (95%CI)*1-49%*Median (months)HR (95%CI)*≥1%*Median (months)HR (95%CI)*<1%*Median (months)HR (95%CI) | 26.3 vs. 13.4 0.62 (0.48-0.81)Same as above--- | 22.0 vs. 10.7 0.56 (0.45-0.70)NR vs. 10.1 0.59 (0.39-0.88)21.9 vs. 12.1 0.62 (0.42-0.92)NR17.2 vs. 10.2 0.52 (0.36-0.74) | 17.2 vs. 11.6 0.71 (0.59-0.86)NR0.64 (0.37-1.10)NR0.57 (0.36-0.90)18.7 vs. 12.8 0.68 (0.53-0.87)15.0 vs. 11.0 0.78 (0.57-1.07) | 17.1 vs. NR vs. 14.9 NR21.2 vs. 18.1 vs. 14.0 Dual/chemo 0.70 (0.55-0.90)Dual/nivo 0.87 (0.68-1.12)NR17.1 vs. 15.7 vs. 14.9 Dual/Chemo 0.79 (97.72%CI 0.65-0.96)Dual/nivo 0.90 (0.76-1.07)- | 17.2 vs. NR vs. 12.2 NR---17.2 vs. 15.2 vs. 12.2 Dual/chemo 0.62 (0.48-0.78)Dual/nivo+chemo 0.77 (0.60-0.98) | 15.6 vs. 10.9 0.66 (0.55-0.80)18.0 vs. 12.6 0.66 (0.44-0.99)15.4 vs. 10.4 0.61 (0.44-0.84)15.8 vs. 10.9 0.64 (0.50-0.82)16.8 vs. 9.8 0.62 (0.45-0.85) |
| **PFS**Median (months)HR (95%CI) | 7.7 vs. 5.5 0.50 (0.39-0.65) | 9.0 vs. 4.9 0.48 (0.40-0.58) | 8.0 vs. 5.1 0.59 (0.49-0.71) | 5.1 vs. 4.2 vs. 5.6NR  | 5.1 vs. 5.6 vs. 4.7 NR | 6.7 vs. 5.0 0.68 (0.57-0.82) |
| **ORR**ITTPD-L1≥50%**CR**ITTPD-L1≥50% | 46%-4.5%- | 31%-0%- | 48%61%1%NR | 19%23%0.5%NR | 63%60%1%NR | 39%33%2%NR | 36%44%6%9% | 28%37%3%5% | 30%35%2%2% | 27%-2%- | 38%-2%- | 23%-1%- | 38%50%2% | 25%31%2% |
| **Time to Response****(months)** | 2.2  | 2.2  | 2.2 | 1.4  | 1.4  | 1.4  | 2.0  | 2.7  | 1.6  | 2.8  | 1.7  | 1.5  | 2.6  | 1.5  |
| **Received 2nd Line Therapy** | 52% | 66% | 45% | 54% | NR | NR | 35% | 44% | 54% | 44% | 41% | 53% | 31% | 53% |
| **Toxicity Profile**All gradeGrade 3/4 | 77%31% | 90%53% | 100%72% | 99%67% | 99%75% | 98%70% | 77%36% | 66%19% | 84%36% | 76%27% | 92%56% | 78%35% | 69%47% | 87%38% |

P = pembrolizumab; N = nivolumab; I = ipilimumab; C = chemotherapy (platinum-doublet)

NR = not recorded; ITT = intention to treat; OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response