Supplemental Online Content

Lamba N, Ott PA, Iorgulescu JB. Use of First-Line Immune Checkpoint Inhibitors and Association With Overall Survival Among Patients With Metastatic Melanoma in the Anti-PD-1 Era. JAMA Netw Open. 2022;5(8):e2225459. doi:10.1001/jamanetworkopen.2022.25459

eTable. Association Between First-Line ICI and OS in Stage IV Melanoma Patients Diagnosed Following FDA Approval, Using Multivariable Cox Regression

This supplemental material has been provided by the authors to give readers additional information about their work.
eTable. Association between first-lineICI and OS in stage IV melanoma patients diagnosed following FDA approval, using multivariable Cox regression

| Landmark timepoint | All | Brain metastases | Liver metastases | High LDH |
|-------------------|-----|------------------|------------------|-----------|
|                   | Landmark 48 days | Landmark 78 days | Landmark 48 days | Landmark 78 days | Landmark 48 days | Landmark 78 days | Landmark 48 days | Landmark 78 days |
| n=                | 3,408 | 3,239 | 1,251 | 1,151 | 802 | 725 | 725 | 488 |
| 1st-line systemic therapy | | | | | | | | |
| Targeted/chemotherapy | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| ICI | 0.76 (0.65-0.88) | <0.001 | 0.72 | 0.62-0.85 | <0.001 | 0.78 | 0.63-0.97 | 0.003 | 0.74 | 0.59-0.94 | <0.001 | 0.82 | 0.63-1.08 | 0.06 | 0.77 | 0.58-1.03 | 0.019 | 0.78 | 0.54-1.22 | 0.07 | 0.77 | 0.52-1.13 | 0.08 |
| Age at diagnosis, yr | <50 | 0.92 | 0.76-1.11 | 0.93 | 0.76-1.12 | 0.85 | 0.65-1.11 | 0.82 | 0.62-1.09 | 1.03 | 0.74-1.43 | 1.05 | 0.74-1.49 | 1.30 | 0.85-1.98 | 1.37 | 0.88-2.14 |
| 50-59 | 0.94 | 0.78-1.13 | 0.89 | 0.73-1.09 | 0.94 | 0.72-1.23 | 0.89 | 0.67-1.18 | 0.91 | 0.65-1.28 | 0.84 | 0.57-1.22 | 1.20 | 0.76-1.87 | 1.03 | 0.63-1.69 |
| ≥60 | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| 70-79 | 1.32 | 1.1-1.57 | 1.29 | 1.07-1.56 | 1.25 | 0.95-1.63 | 1.19 | 0.89-1.58 | 1.41 | 1.01-1.96 | 1.44 | 1.01-2.06 | 1.27 | 0.78-2.06 | 1.30 | 0.78-2.17 |
| ≥80 | 1.60 | 1.29-1.98 | 1.55 | 1.24-1.94 | 1.28 | 0.88-1.88 | 1.13 | 0.74-1.73 | 1.29 | 0.86-1.94 | 1.35 | 0.87-2.09 | 1.72 | 0.99-2.97 | 1.65 | 0.91-2.98 |
| Charlson-Deyo comorbidity index | 0 | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| 1 | 1.06 | 0.88-1.27 | 1.09 | 0.9-1.32 | 1.00 | 0.76-1.31 | 1.04 | 0.78-1.39 | 0.98 | 0.69-1.39 | 0.98 | 0.68-1.43 | 0.88 | 0.56-1.38 | 0.91 | 0.56-1.47 |
| ≥2 | 1.40 | 1.13-1.73 | 1.38 | 1.1-1.74 | 1.18 | 0.85-1.64 | 1.18 | 0.83-1.67 | 1.23 | 0.79-1.9 | 1.14 | 0.7-1.86 | 1.07 | 0.58-1.99 | 1.07 | 0.55-2.1 |
| Radiotherapy | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.32 | 1.13-1.55 | 1.32 | 1.12-1.55 | 1.35 | 1.05-1.73 | 1.36 | 1.04-1.77 | 1.31 | 1.1-1.72 | 1.26 | 0.94-1.69 | 1.36 | 0.95-1.94 | 1.31 | 0.89-1.92 |
| Year of diagnosis, per yr | 0.95 | 0.87-1.02 | 0.94 | 0.87-1.03 | 1.00 | 0.89-1.13 | 1.01 | 0.89-1.15 | 0.95 | 0.82-1.1 | 0.96 | 0.82-1.12 | 1.02 | 0.85-1.23 | 0.99 | 0.81-1.21 |
| Surgery of non-primary site | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 0.64 | 0.55-0.75 | 0.68 | 0.58-0.79 | 0.62 | 0.5-0.77 | 0.67 | 0.54-0.84 | 0.71 | 0.51-1 | 0.76 | 0.53-1.06 | 0.53 | 0.35-0.81 | 0.56 | 0.36-0.87 |
| Brain metastases | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.69 | 1.44-1.98 | 1.63 | 1.38-1.92 | All have brain mets | All have brain mets | 1.43 | 1.08-1.89 | 1.40 | 1.04-1.9 | 1.14 | 0.8-1.63 | 1.14 | 0.78-1.66 |
| Lung metastases | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.10 | 0.97-1.25 | 1.06 | 0.93-1.21 | 1.19 | 0.98-1.45 | 1.15 | 0.93-1.42 | 1.05 | 0.82-1.34 | 0.97 | 0.74-1.26 | 1.22 | 0.89-1.68 | 1.14 | 0.81-1.59 |
| Other organ metastases | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.08 | 0.95-1.23 | 1.03 | 0.9-1.18 | 1.01 | 0.82-1.23 | 0.97 | 0.78-1.2 | 0.99 | 0.78-1.25 | 0.92 | 0.71-1.2 | 1.08 | 0.8-1.46 | 1.01 | 0.73-1.4 |
| Distant LN metastases | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.10 | 0.96-1.26 | 1.11 | 0.96-1.28 | 1.08 | 0.87-1.35 | 1.09 | 0.86-1.38 | 0.99 | 0.78-1.27 | 0.99 | 0.76-1.29 | 1.11 | 0.81-1.51 | 1.12 | 0.8-1.57 |
| Liver metastases | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.50 | 1.3-1.73 | 1.44 | 1.24-1.68 | 1.35 | 1.08-1.7 | 1.31 | 1.02-1.68 | All have liver mets | All have liver mets | 1.19 | 0.86-1.64 | 1.15 | 0.81-1.62 |
| Bone metastases | No | Ref | Ref | Ref | Ref | Ref | Ref | Ref | Ref |
| Yes | 1.57 | 1.36-1.81 | 1.57 | 1.35-1.83 | 1.37 | 1.1-1.72 | 1.38 | 1.08-1.76 | 1.49 | 1.18-1.88 | 1.50 | 1.16-1.93 | 1.57 | 1.15-2.15 | 1.55 | 1.11-2.17 |

ICI = immune checkpoint inhibitor; HR = hazard ratio; CI = confidence interval; LN = lymph node

P values were only calculated and displayed for the primary association of interest, that between first-line ICI and OS. 99% CIs are reported for all other associations.

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