Background Best practice in surveillance imaging for survivors after immune checkpoint inhibitors (CPI) remain poorly defined for stage 3-4 aMEL; KPNC oversees care for 4 million patients and has 300 new diagnoses of aMEL per year. Follow-up after CPI is coordinated in KPNC via care pathways using national guidelines.

Methods We report a retrospective study of patients treated between 2014 and 2018 for aMEL with CPI. Data was obtained by chart review. Patients were included who received anti-PD1, anti-CTLA4, or combination; had ≥1 dose of any-line palliative (pTX) or adjuvant therapy (adjTX); and had ≥1 year of follow-up after treatment, and imaging response (SD/PR/CR) or ≥6 months without recurrence if after adjTX. Symptomatic versus asymptomatic progression was defined by evidence of documentation of symptoms at time of imaging. Events from patients who had >1 line of CPI therapy were counted separately. Log-rank test was used to determine Kaplan-Meier survival estimates, and rates were calculated per 100 person-months.

Results 176 patients met inclusion criteria. These patients underwent 191 lines of therapy (69 adjTX and 122 pTX). Progression after therapy occurred in 29 lines of treatment (42%) after adjTX, of these 62% were symptomatic. 51 (41.8%) patients relapsed after pTX and 44% were symptomatic. Comparing asymptomatic and symptomatic progression, there were no differences in risk of relapse after adjTX (p=0.14) or pTX (p=0.73). Within adjTX, patients with asymptomatic recurrences had lower all-cause mortality (ACM) than those with symptoms (Relative Risk (RR) 0.6 [0.0-1.3] vs 1.9 [0.8-3.0], p=0.03) and lower melanoma-specific mortality (MSM) (RR 0.2 [0.0-0.6] vs 1.2 [0.3-2.1], p=0.03 for MSM). No differences were detected for ACM and MSM for patients receiving in pTX with asymptomatic versus symptomatic recurrence (ACM RR 1.9 [1.0-2.9] in asymptomatic recurrence vs 2.8 [1.4-4.2] in symptomatic, p=0.15 for ACM and; MSM RR 1.6 [0.7-2.4] vs 2.4 [1.2-3.7], p=0.12 for MSM). There were differences in ACM (p=0.02) and MSM survival (p=0.01) in adjTX but not in pTX (ACM p=0.90; MSM p=0.79).

Conclusions Our study finds identification of asymptomatic relapse has survival benefit in the curative setting but not for aMEL treated with palliative intent. This finding is likely because curative therapy can be offered if relapse is identified early for resectable disease. Our study findings suggests a symptom-based imaging surveillance strategy similar to that used in histologies with effective systemic therapy is effective (e.g. lymphoma, breast cancer) could potentially be used for melanoma. Prospective study is needed to further guide clinical practice.