Supplemental Table S1. Clinicopathologic features of archival, histologically aggressive BCCs.

Characteristic	Patients (n=34)
Age, years	
Median (range)	66 (45-96)
Sex, n (%)	
Male	27 (79%)
Female	7 (21%)
Size, n (%)	
< 1 cm Head and Neck	2 (5.9%)
≥ 1cm Head and Neck	25 (73.5%)
< 2 cm Trunk/Extremity	3 (8.8%)
≥2 cm Trunk/Extremity	4 (11.8%)
Location, n (%)	
Head and Neck	27 (79%)
Trunk/Extremity	7 (21%)
Perineural invasion, n (%)	
Yes	20 (59%)
No	14 (41%)
Invading bone, n (%)	
Yes	3 (9%)
No	31 (91%)
Recurred locally, n (%)	
Yes	8 (23.5%)
No	21 (61.8%)
N/A	5 (14.7%)
Metastasis, n (%)	
Yes	4 (11.8%)
No	25 (73.5%)
N/A	5 (14.7%)
Prior systemic therapy, n (%)	
No	30 (88%)
Yes (vismodegib)	4 (12%)

Supplemental Figure S1.

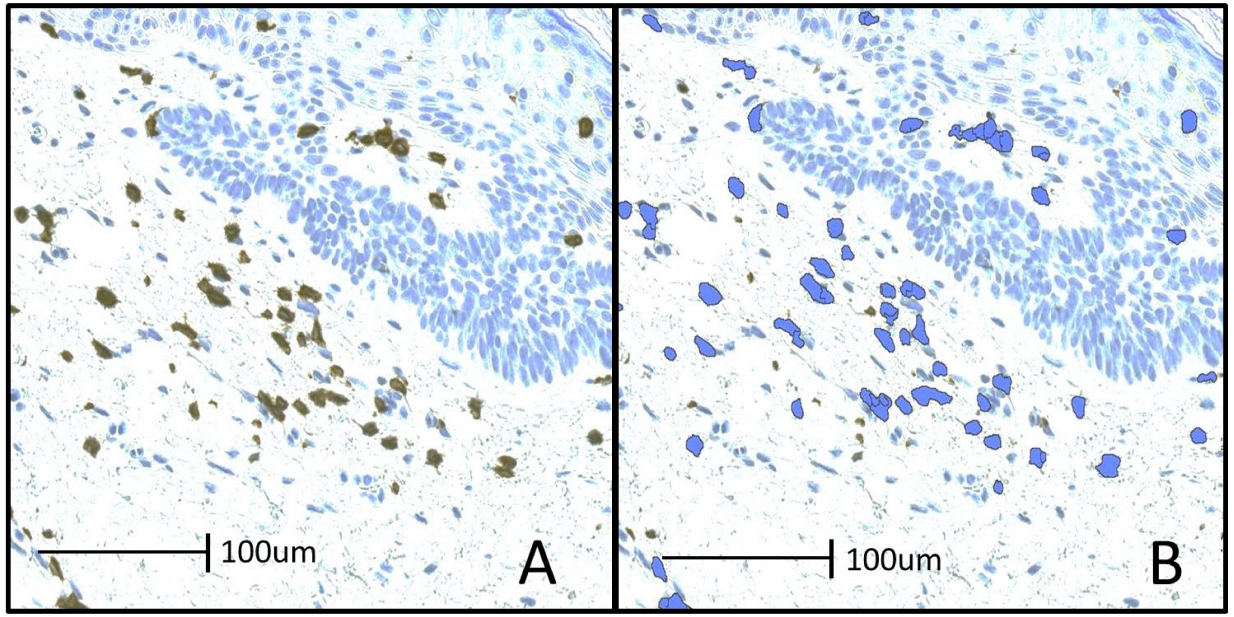


Figure S1. **Computer assisted quantification of IHC markers. (A)** IHC for CD3 (brown chromogen) **(B)** quantification of IHC staining in blue (algorithm counts all positive cells with a nucleus in the field of interest).

Supplemental Figure S2.

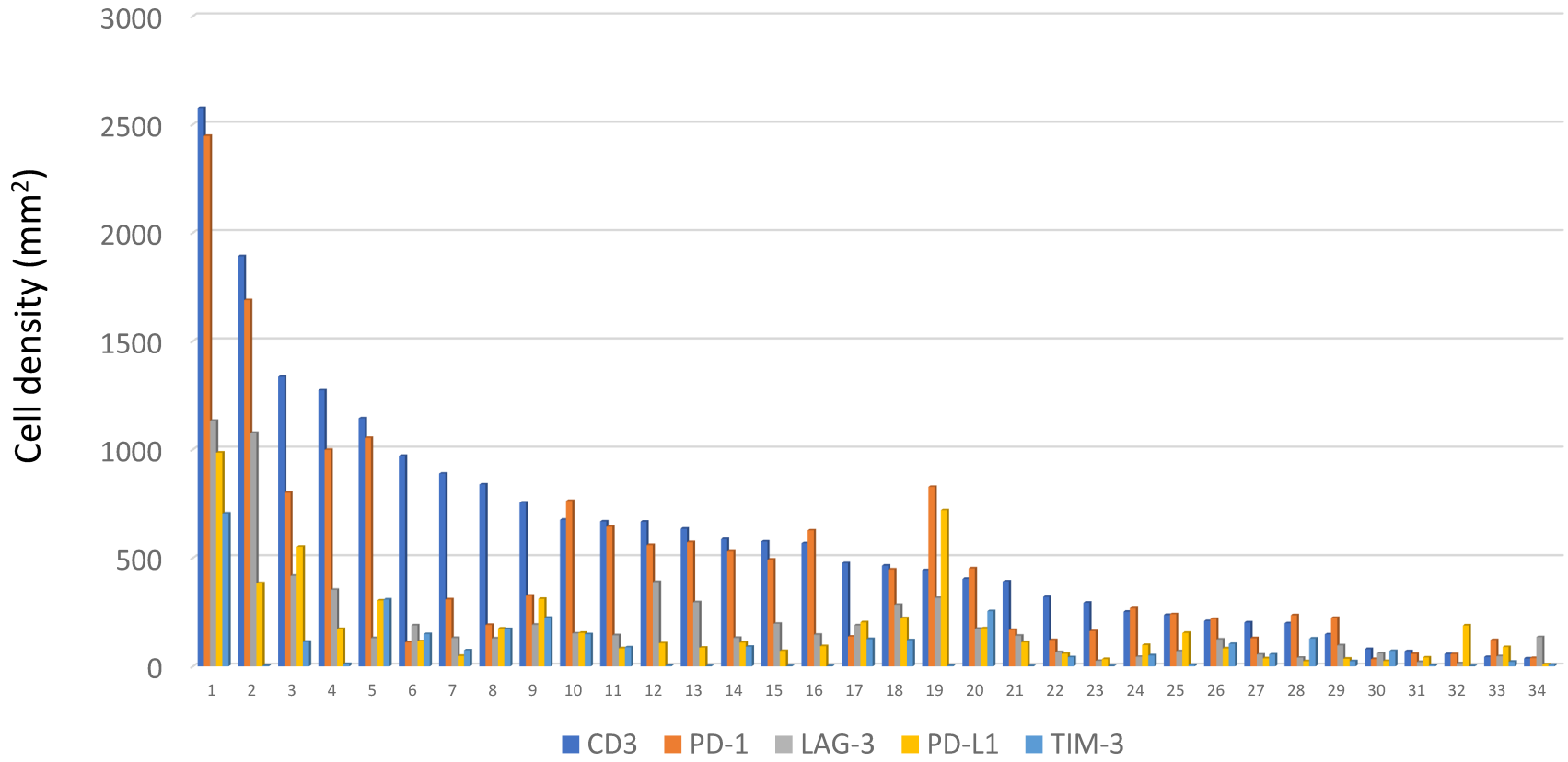
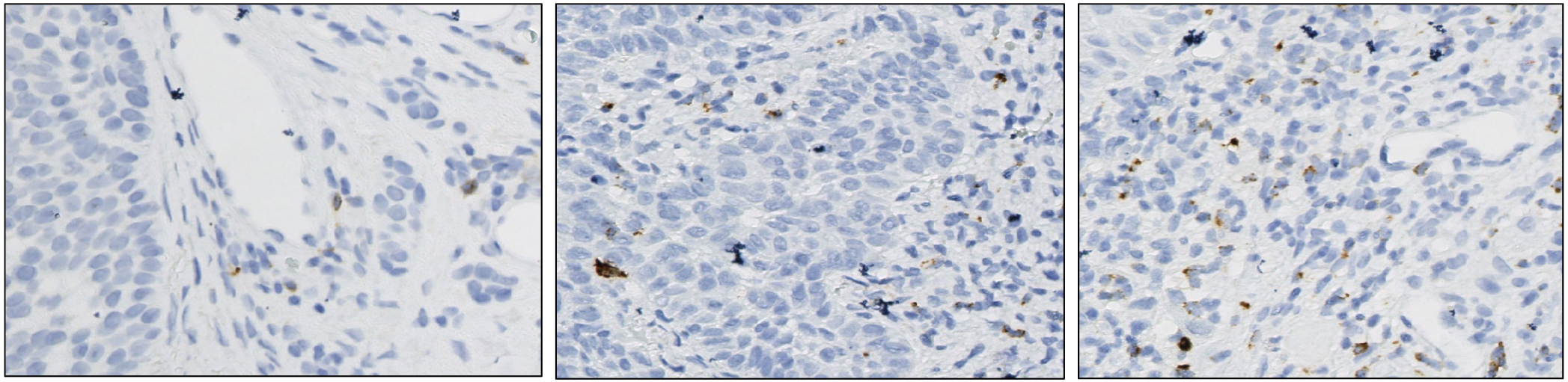


Figure S2. Correlation of immune cell subset densities and checkpoint marker expression on lymphocytes with degree of T-cell infiltration and with each other. PD-1+ densities were consistently the highest, followed by LAG-3 and PD-L1, at ~50% and ~35% of the levels observed for PD-1, respectively. Each set of bars represents an individual specimen. Cases demonstrating constitutive component of checkpoint expression are graphically distinct, e.g. PD-1 and PD-L1 densities are higher than CD3 densities as is seen in specimens such as 16, 19, and 32.

Supplemental Figure S3.



Pre-treatment

On-treatment
(4 weeks on anti-PD-1)

On-treatment
(16.5 months on anti-PD-1)

Figure S3. IHC for LAG-3 performed on serial biopsies from this patient (pre-treatment, 4 weeks on-treatment, and 16.5 months after the first dose of anti-PD-1) showed 1%, 5%, and 10% expression in ICs, respectively. This graduated increase in LAG-3 checkpoint expression after anti-PD-1 therapy lends support for coordinated immunosuppression.