



SKIN CANCER (OTHER THAN MELANOMA)

## PEMBROLIZUMAB WITH OR WITHOUT VISMODEGIB FOR ADVANCED BASAL CELL CARCINOMA: AN INVESTIGATOR-INITIATED, PROOF-OF-CONCEPT STUDY

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**Introduction:** A significant proportion of advanced basal cell carcinomas (BCCs) are refractory, resistant or recur after Hedgehog pathway inhibition or other therapies. As BCCs have particularly high mutational burdens and can express Programmed Death ligand (PDL)-1, we performed a proof-of-concept study of the PD-1 inhibitor, pembrolizumab, with or without vismodegib for advanced BCCs.

**Objective:** To assess the efficacy and safety of pembrolizumab for advanced BCCs

**Materials and Methods:** This single-institution, two-cohort, non-randomized study enrolled patients with advanced BCCs. Eligible patients received pembrolizumab 200mg every 3 weeks as monotherapy or in combination with vismodegib 150mg daily. Responses and treatment-emergent adverse events (AEs) were assessed in all patients who received at least one dose of pembrolizumab. The trial is registered with ClinicalTrials.gov as NCT02690948

**Results:** Sixteen eligible patients were enrolled and were evaluable. Overall response rate (ORR) was 38% (6/16) [95% confidence interval (CI): 15-65%],  $p=0.003$ , at 18 weeks. ORR for pembrolizumab monotherapy group was 44% (4/9) [95%CI: 14-79%],  $p=0.008$  and pembrolizumab plus vismodegib group was 29% (2/7) [95%CI: 4-71%],  $p=0.15$ . Three patients (2 with partial response and 1 with stable disease) continued to receive off-label treatment through their community oncologists and achieved complete response after study discontinuation. One-year progression-free survival probability was 70%, and one-year overall survival probability was 94% for all evaluable subjects. There was no significant correlation between pre-pembrolizumab PDL-1 expression and the best percentage change in BCC diameter. There were no life-threatening AEs or deaths.

**Conclusions:** The robust response rate of advanced BCCs to pembrolizumab suggests that





pembrolizumab has clinical activity against advanced BCCs. This, together with the acceptable side-effect profile suggests pembrolizumab may be a meaningful therapeutic option. Multi-institutional studies are underway to further investigate the effects of PD-1 inhibition on advanced BCCs.

