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Pembrolizumab for advanced basal cell carcinoma: An investigator-initiated, proof-of-concept study

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To the Editor:

Case reports[1] and the high tumor mutational burden[2] of basal cell carcinomas (BCCs) compared with other tumor types suggest that programmed death-ligand 1 (PD-L1) inhibitors may be active against advanced BCCs. Many advanced BCCs are refractory to[3] or are recurrent[4] after hedgehog pathway inhibitors, and therefore PD-L1 inhibitors could be a useful therapeutic option. We present a proof-of-principle, nonrandomized, open-label study of pembrolizumab (200 mg intravenously every 3 weeks), with or without vismodegib (150 mg orally daily), for eligible subjects with advanced BCCs. The primary outcome was the overall response rate (ORR) for all evaluable subjects at 18 weeks.

Sixteen participants, 9 receiving pembrolizumab monotherapy and 7 receiving pembrolizumab plus vismodegib, were evaluable by the revised Response Evaluation Criteria In Solid Tumors[5] (version 1.1) at data cutoff. The ORR for all evaluable subjects was 38% (6/16 patients; 95% confidence interval 15–65%; $P = .003$) at 18 weeks (Table I, Fig 1). The ORR at 18 weeks for pembrolizumab monotherapy group was 44% (4/9 patients; 95% confidence interval 14–79%; $P = .008$), and for the dual therapy group was 29% (2/7 patients; 95% confidence interval 4–71%; $P = . 15$).

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The other authors have no conflicts of interest to disclose.

This study is subject to Stanford Human Subjects Approval Protocol 34925 and is listed at clinicaltrials.gov ().

The median time to response for all responders (n = 6) was 10.4 weeks (range 8.4–17.4 weeks). The median duration of response for all responders (n = 6) was 67.3 weeks (range 28.0–82.0 weeks; Table I).

One-year progression-free survival probability was 70%, and the 1-year overall survival probability was 94% for all evaluable subjects (n = 16; Table I).

Before pembrolizumab, 29% (2/7 patients) expressed PD-L1 at ≥1% of tumor cells. There was no significant correlation between prepembrolizumab PD-L1 expression and best percentage change in BCC diameter.

There were no life-threatening adverse events (AEs) or deaths during the study. Three severe (grade 3) AEs occurred out of 98 AEs from 16 participants. Only 1 of the severe AEs, hyponatremia, was attributed to pembrolizumab. There were 23 immune-related AEs, with dermatitis and fatigue as the most common (all grade 1 or 2), and only 1 severe immune-related AE (the aforementioned hyponatremia).

As a proof-of-principle study, we conclude that pembrolizumab is active against BCCs. Although the 2 groups were not directly compared, the response rate of the pembrolizumab plus vismodegib group was not superior to the monotherapy group. The lack of life-threatening AEs or death suggests that pembrolizumab has a reasonable safety profile in patients with BCC.

This study is limited by its sample size, because advanced BCCs are an uncommon disease. Nevertheless, the efficacy and safety data presented here could be used in future meta-analyses and compared with forthcoming multi-institutional studies on PD-L1 inhibitors against advanced BCCs.

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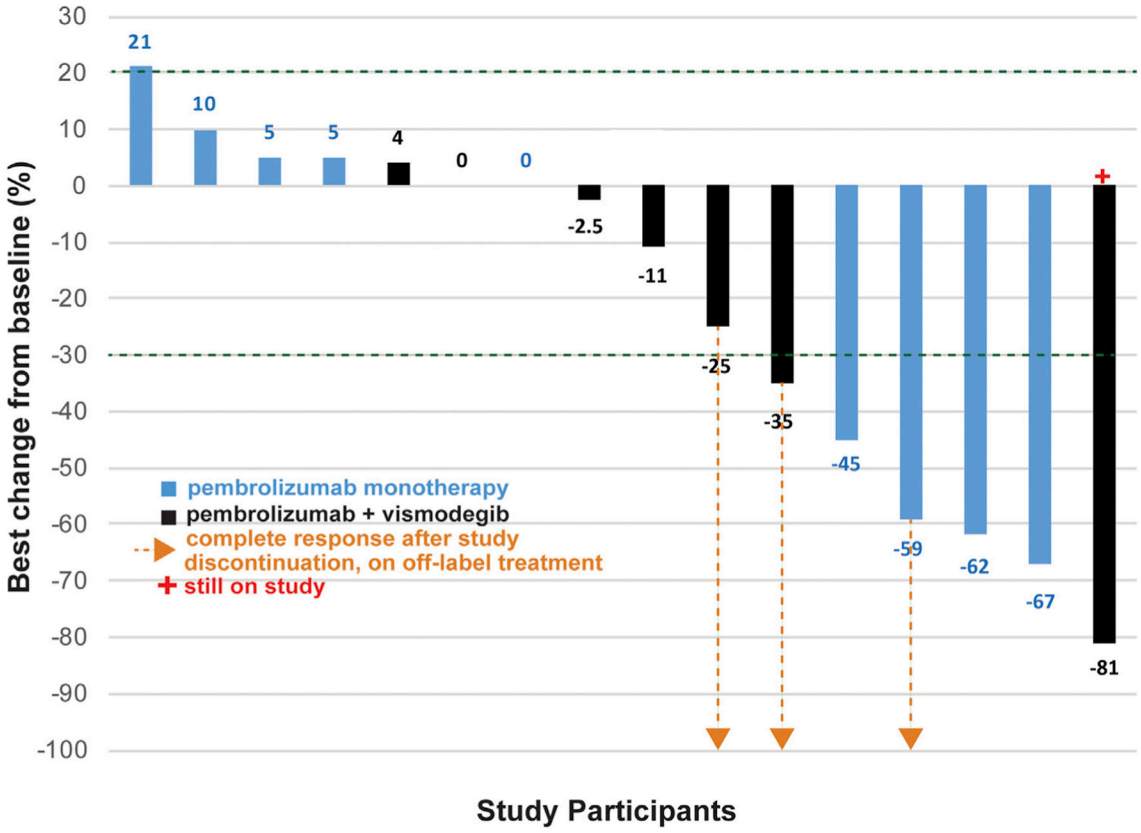

Fig 1.

Waterfall plot showing best percent change in the diameter of targeted basal cell carcinoma lesions from baseline for all evaluable subjects. The dotted arrows indicate 3 subjects who achieved complete response after study discontinuation, based on imaging and clinical documentation.

Table I.

Primary and secondary outcomes

Outcome	All evaluable participants (N = 16)	Pembrolizumab monotherapy (n = 9)	Pembrolizumab plus vismodegib (n = 7)
Overall response rate (range), n	38% (15–65%), 6	44% (14–79%), 4	29% (4–71%), 2
One-year PFS probability, %	70	62	83
One-year OS probability, %	94	89	100
Median treatment duration, weeks (range)	18.5 (5.9–73.0)	19.0 (10–73.0)	18.0 (5.9–38.6)
Median time to response, weeks (range), n	10.4 (8.4–17.4), 6	12.4 (8.4–17.4), 4	10.3 (8.7–11.9), 2
Median duration of response, weeks (range), n	67.3 (28.0–82.0), 6	67.6 (31.4–82.0), 4	52.8 (28.0–77.6), 2
Median time from pembrolizumab start date to next treatment start date, weeks (range), n	21.9 (6.1–43.3), 6	21.9 (15.4–43.3), 4	19.2 (6.1–32.3), 2

Overall response rates were calculated at the 18-week time point. One-year progression-free survival and overall survival probabilities were calculated using the KaplaneMeier method.

OS, Overall survival; *PFS*, progression-free survival.