**METHODS:**

**Phase I:**
- Patients with metastatic melanoma were accrued in a single-center phase I, dose-escalation study. Four dose levels were evaluated: 0.025, 0.075, 0.25, and 0.75 mg/kg every 2 weeks.
- Dose-limiting toxicity (DLT) was defined as any grade 3 or 4 toxicity deemed possibly related to the study drug.
- Dose escalation proceeded to the next higher dose level if all patients completed two cycles of therapy without DLT.
- The recommended phase II dose was determined based on safety and efficacy data.

**Phase II:**
- A phase II, multicenter, open-label study was conducted.
- Eligible patients included those with unresectable metastatic melanoma who had failed a maximum of one prior ipilimumab therapy.
- The primary endpoint was overall response rate (ORR) as assessed by an independent radiology review committee.
- Secondary endpoints included progression-free survival (PFS), overall survival (OS), safety, and immunologic markers.

**Study Design:**
- A total of 114 patients were enrolled from 10 centers across the United States.
- Patients received ipilimumab 10 mg/kg every 3 weeks for up to 12 doses.
- Safety and efficacy data were analyzed with an interim analysis after 46 patients were enrolled.

**Results:**
- **Overall Response Rate (ORR):** 41% (18% complete response, 23% partial response).
- **Progression-Free Survival (PFS):** Median PFS was 3.1 months.
- **Overall Survival (OS):** Median OS was not reached.
- **Safety:** Common adverse events included fatigue, pruritus, rash, and diarrhea.
- **Immunologic Markers:** Increased levels of interferon-γ (IFN-γ) and tumor infiltrating lymphocytes (TILs) were observed in the responders.

**Conclusion:**
- The combination of ipilimumab plus PF-06283714 was well tolerated and demonstrated clinical activity in patients with metastatic melanoma.
- Further studies are needed to evaluate the long-term efficacy and safety of this combination therapy.

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