Background
- Immune checkpoint inhibitors are a standard of care for patients with metastatic melanoma, demonstrating durable survival benefit.
- High-dose interleukin-2 (IL-2) monotherapy has shown efficacy, including complete responses, in patients with metastatic melanoma. However, its use is limited by toxicities and inpatient drug administration.
- Bempegaldesleukin is a CD122-preferential IL-2 pathway agonist designed to provide sustained signaling through the IL-2βγ receptor (Figure 1).

![Figure 1. Bempegaldesleukin preferential signaling through the IL-2βγ receptor pathway](image)

**Figure 1.** Bempegaldesleukin preferential signaling through the IL-2βγ receptor pathway

### PIVOT IO 001 Rationale
- In preclinical studies, the combination of bempegaldesleukin and an anti-programmed death 1 (PD-1) checkpoint inhibitor demonstrated durable survival benefit in comparison with either therapy alone.

#### PIVOT-02 (NCT02983045) bempegaldesleukin + NIVO combination study
- **Primary objective:** Efficacy and safety of bempegaldesleukin + NIVO in patients with previously untreated, metastatic melanoma.
- **Inclusion criteria:**
  - Treatment-naive patients with metastatic melanoma, renal cell carcinoma, or urothelial carcinoma.
  - Metastatic melanoma: presence of ≥ 1 measurable lesion.
- **Exclusion criteria:**
  - Prior treatment with IL-2, IL-12, or IL-21.
  - Active brain metastases or leptomeningeal disease.
- **Primary endpoint:** ORR.
- **Secondary endpoints:** PFS, OS, DOR, and safety.

### PIVOT IO 001 Objective
- PIVOT IO 001 is designed to evaluate the efficacy and safety of bempegaldesleukin + NIVO in patients with previously untreated, metastatic melanoma.

### PIVOT IO 001 Study Design
- **Population:** Treatment-naive patients with metastatic melanoma.
- **Stratification factors:** PD-L1 status, AJCC stage.
- **Primary endpoint:** ORR.
- **Secondary endpoints:** PFS, OS, DOR, and safety.

### Results
- **Overall response rate (ORR):** 20.5% (95% CI: 13.7–28.6%) with bempegaldesleukin + NIVO.
- **Confidence intervals (CIs):**
  - ORR: 13.4–28.4%.
  - PD-L1 negative: 16.5–25.4%.
  - PD-L1 positive: 37.5–58.5%.
- **Key patient inclusion and exclusion criteria:**
  - Inclusion criteria:
    - **ECOG PS ≤ 1:** adults aged 18 years or older.
    - **Lansky performance score ≥ 90%:** ages 12 years or older.
  - Exclusion criteria:
    - Active brain metastases or leptomeningeal disease.
    - Uveal melanoma.

### References
2. Hurwitz ME, et al. Poster presentation at Genitourinary Cancers Symposium (ASCO GU); February 14–16, 2018; Orlando, FL, USA. Abstract 415A.

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- The study is supported by Bristol-Myers Squibb.

**Figure 2.** Best percent change from baseline in target lesion size with bempegaldesleukin + NIVO in patients with previously untreated, metastatic melanoma.

**Figure 3.** PIVOT IO 001 study design.

**Figure 4.** Countries participating in PIVOT IO 001.