

**Article details**

**Title of article**  
Bempegaldesleukin plus nivolumab in untreated, unresectable or metastatic melanoma: Phase III, PIVOT IO 001 study design

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**Trial registration number**  
NCT03635983

**Key eligibility criteria**

- ≥12  
12 years of age
- Histologically confirmed unresectable or metastatic melanoma
- Treatment-naive, with the exception of prior adjuvant and/or neoadjuvant treatment
- 0 or 1  
ECOG PS 0 or 1 in adult patients; Lansky performance score of 80% (patients 12-17 years of age)
- No active brain metastases or leptomeningeal metastases; uveal melanoma; or an active, known or suspected autoimmune disease

**Primary objectives/rationale**

**Primary objective**  
Compare ORR, PFS and OS of combination BEMPEG plus NIVO versus NIVO alone in patients with previously untreated, unresectable or metastatic melanoma

**Secondary key objectives**

- Compare safety and tolerability of combination BEMPEG plus NIVO with that of NIVO monotherapy
- Compare additional efficacy measures of combination BEMPEG plus NIVO with that of NIVO monotherapy
- Assess association between PD-L1 tumor expression on tumor cells ( 1% or <1%/indeterminate) and efficacy measures, including PFS, ORR and OS

**Study design and treatment**

**Target enrollment: 764**

**Screening**  
**Population:**  
• Treatment-naive  
• Unresectable or metastatic melanoma  
**Stratification factors:**  
• PD-L1 status  
• BRAF mutation status  
• AJCC M stage

**Randomization 1:1**

**Treatment**  
Patients will receive either

- BEMPEG 0.006 mg/kg iv. Q3W plus NIVO 360 mg iv. Q3W
- NIVO 360 mg iv. Q3W

**Follow-up**  
Follow-up for safety, RECIST v1.1 progression and survival  
The total duration of the study is up to 5 years from the randomization of the last participant, or until the time of primary OS analysis, whichever occurs later

Treat until RECIST v1.1 progression or unacceptable toxicity

**Outcome measures/endpoints**

**Primary endpoints**  
ORR by BICR, PFS by BICR, OS

**Secondary endpoints**  
CBR, DoR, TTR; ORR, PFS, OS in PD-L1 biomarker population; investigator-assessed ORR and PFS

**Exploratory endpoints**  
PK and immunogenicity parameters, PRO

**Glossary**

AJCC: American Joint Committee on Cancer; BEMPEG: Bempegaldesleukin; BICR: Blinded independent central review; CBR: Clinical benefit rate; DoR: Duration of response; ECOG PS: Eastern Cooperative Oncology Group performance status; IL-2: Interleukin-2; iv.: Intravenous; LDH: Lactate dehydrogenase; M: Metastatic; NIVO: Nivolumab; ORR: Objective response rate; OS: Overall survival; PD-L1: Programmed death ligand 1; PFS: Progression-free survival; PK: Pharmacokinetic; PRO: Patient-reported outcomes; Q3W: Every 3 weeks; RECIST v1.1: Response Evaluation Criteria In Solid Tumors; TTR: Time to response