
Eligibility criteria

Figure 3. PIVOT-12 study design – adjuvant therapy with BEMPEG plus NIVO in completely resected cutaneous melanoma at high risk for recurrence

**BACKGROUND**

Adjuvant treatment of cutaneous melanoma

- Locally and regionally advanced cutaneous melanomas with lymph node involvement are at high risk for recurrence following surgical resection, which is associated with poor survival outcomes
- Despite checkpoint inhibitor therapy as an effective adjuvant treatment option for resected stage II or IV cutaneous melanoma, up to one-third of patients will have experienced disease recurrence by 4 years
- There is an unmet need for novel adjuvant therapies that combine the potential to reduce or delay recurrence and extend survival in patients with resected cutaneous melanoma

**BEMPEG signals preferentially through the IL-2R pathway**

- Bempegaldesleukin (NKTR-214) preferentially engages IL-2R pathway agonist that has been engineered to deliver a controlled, sustained, and preferred IL-2 pathway signal
- In animal models and in patients with cancer, BEMPEG induced increased proliferation and infiltration of CD8+ T cells without expansion of unwanted regulatory T cells in the tumor microenvironment (Figure 1)
- In addition, BEMPEG has been shown to up-regulate PD-1, as well as its ligand PD-L1

**PIVOT-12: A PHASE 3 TRIAL OF BEMPEG PLUS NIVO IN ADJUVANT MELANOMA**

**Study design**

PIVOT-12 (NCT03151814) is a phase 3, global, multicenter, randomized, open-label study of BEMPEG plus NIVO as an adjuvant treatment for patients with completely resected cutaneous melanoma at high risk for recurrence (Figure 2).

- Approximately 950 patients will be randomized 1:1:1 to receive adjuvant BEMPEG plus NIVO (Arm A; 3-week cycle) or NIVO alone (Arm B; 4-week cycle)
- Patients will be treated for up to 1 year or until disease recurrence, death, unacceptable toxicity, decision by the investigator or patient to discontinue treatment, withdrawal of consent, loss to follow-up, or study termination

**Objectives**

**Primary**

- Compare the efficacy of BEMPEG plus NIVO versus NIVO alone by assessing RFS per BICR, up to approximately 6 months

**Secondary**

- Evaluate overall survival
- Evaluate OMF in patients with stage III disease at study entry
- Evaluate RFS per investigator assessment
- Assess the safety and tolerability of BEMPEG plus NIVO using the CTCAE v4.0
- Describe changes from baseline in patient-reported outcomes as assessed by the QLQ-C30 questionnaire
- Assess the predictive strength of PD-L1+ expression in a biomarker-relied on a BICR

**Status**

- The PIVOT-12 study is open for enrollment, with close to 100 active or planned sites globally (Figure 4)
- Please visit ClinicalTrials.gov and search for NCT03151814 to find out the latest information on this study

**REFERENCES**


**ABBREVIATIONS**

- TME, tumor microenvironment
- PD-1, programmed death-1
- PD-L1, programmed death-ligand 1
- NIVO, nivolumab
- RFS, recurrence-free survival
- BICR, blinded independent central review
- CR, complete response
- CI, confidence interval
- mo, months
- NE, not estimable
- ORR, objective response rate
- PFS, progression-free survival
- PR, partial response
- RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

**KEY INCLUSION CRITERIA**

- Age ≥18 years
- Resected cutaneous melanoma with no evidence of disease* – Stage IIIA (lymph node metastases ≤1 cm)
- Stage IIIB/C/D
- Stage IV (M1a/b/c/d)

**KEY EXCLUSION CRITERIA**

- Prior treatment for melanoma (except surgery for melanoma and/or adjuvant radiation for central nervous system metastasis)
- Prior treatment with interferon, interleukins (takasilogene, IL-12 directed therapy, anti-IFN-1, and/or rIL-2), IL-15, and/or CD137, or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways
- History of response to any previous treatment for cancer
- Active, known, or suspected autoimmune disease
- History of another cancer (other than skin cancer or non-melanoma skin cancer, and certain precancerous conditions including: stage 0 or IA c憒arcinoma in situ and endometrial and prostate cancers that have been apparently cured)

**Population**

N=950

**PIVOT-12: A Phase 3 randomized study of adjuvant bempegaldesleukin (BEMPEG) plus nivolumab (NIVO) versus NIVO in completely resected cutaneous melanoma at high risk for recurrence**

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