Background

- ICI and targeted therapies have transformed the treatment landscape of advanced (unresectable or metastatic) melanoma; however, most patients receiving frontline ICI progress within a year.
- Further, 40%–65% of patients have disease that is primary resistant to ICI, and 30%–40% of patients have secondary-resistant disease.
- Novel early-line therapies are needed to improve the rate of deep and durable responses and to increase the proportion of patients with long-term benefit.
- Lifileucel, an autologous TIL cell therapy, has demonstrated potentially meaningful clinical activity in patients with advanced melanoma in the post-ICI setting.

The combination of lifileucel with pembrolizumab has the potential for enhanced antitumor activity through the addition of PD-1 blockade, allowing for optimal engraftment, increased cytotoxicity, and intratumoral expansion of the infused lifileucel product.

- Continued pembrolizumab therapy after lifileucel infusion is expected to perpetuate the antitumor effect.
- Earlier-line treatment with lifileucel plus pembrolizumab demonstrated encouraging efficacy in patients with ICI naïve advanced melanoma in Cohort 1A of the Phase 2 IOV-COM-202 study.
  - Investigator-assessed ORR of 67%.
  - CR rate of 25%.

Study Design and Treatment Regimen

**Figure 1. TILVANCE-301 Study Design**

**Figure 2. TILVANCE-301 Treatment Schema**

**Figure 3. Optional Crossover Schema for Participants in Arm B With Progression on Pembrolizumab Monotherapy**

TILVANCE-301 Study Overview

- **TILVANCE-301 (NCT05279704)** is a Phase 3, multicenter, randomized, open-label, parallel-group, treatment study to assess the efficacy and safety of lifileucel in combination with pembrolizumab compared with pembrolizumab alone in patients with untreated unresectable or metastatic melanoma.

Key Eligibility Criteria

**Inclusion Criteria**

- Melanoma of uveal/ocular origin.
- Symptomatic untreated brain metastases.
- Prior therapy for metastatic disease or >1 prior line of treatment in any setting.
  - Patients completing 1 prior line of neoadjuvant/adjuvant therapy with no progression for ≥6 months are allowed (except for patients with BRAF V600 mutation receiving ICI alone as prior neoadjuvant/adjuvant therapy).
  - Active medical illnesses (eg, systemic infections; seizure disorders; coagulation disorders; other active major medical illnesses of the cardiovascular, respiratory, or immune systems).
- Any form of primary or acquired immunodeficiency (eg, SCID; AIDS).
- Other primary malignancy in the last 3 years.
- Allogeneic cell or organ transplant.

**Exclusion Criteria**

- Uveal/ocular melanoma.
- Patients with untreated or metastatic melanoma will be randomized (1:1) to either Arm A or Arm B.
- Optional crossover* Schema for Participants in Arm B With Progression on Pembrolizumab Monotherapy.

**Abbreviations**

AIDS, acquired immunodeficiency syndrome; BIRC, blinded independent review committee; baseline, baseline for the crossover period; C/I, eligibility, eligibility assessments and imaging for the crossover period; CR, complete response; OR, objective response; OS, overall survival; PD, progressive disease.

**References**