**Background**

- IC1 and targeted therapies have transformed the treatment landscape of advanced (unresectable or metastatic) melanoma; however, most patients receiving IC1 progress within a year.
- Further, 40%–65% of patients have disease that is resistant to IC1 and 30%–40% of patients have secondary-resistant disease.
- Recent early-phase trials are needed to improve the rate of deep and durable responses to increase the proportion of patients with long-term benefit.

- Lifileucel, an antigen-specific T-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 IC1 blockade allowing for optimal engagment, increased cytotoxicity, and intratumoral expansion of the induced T-cell product.

- Continued pembrolizumab therapy after lifileucel infusion is expected to perpetuate the antitumor effect.

- Early-phase treatment with lifileucel plus pembrolizumab demonstrated encouraging efficacy in patients with IC1-refractory melanoma in Current IT of the Phase 2 104CM-202 study.

- Investigator-assessed ORR of 67%.

- CR rate of 26%.

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**TILVANCE-301 Study Overview**

- TILVANCE-301 (NCT05779046) 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 unresectable or metastatic melanoma.

- Patients randomized to Arm B who receive pembrolizumab and experience confirmed progressive disease, verified by BIRC, have the option to receive lifileucel monotherapy as the immediate next line of treatment.

- The study will enroll globally.

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**Study Design and Treatment Regimen**

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

- Eligibility (cEligibility)
- Imaging assessments and imaging
- Baseline assessments completed

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

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

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**Key Inclusion and Exclusion Criteria**

**Inclusion Criteria**

- Histologically or pathologically confirmed diagnosis of Stage IIIIC, IV, or IV unresectable or metastatic melanoma.
- Age 18–70 years
- Patients >70 years of age may be allowed (after discussion with the medical monitor).
- ECOG PS 0 or 1 and estimated life expectancy >6 months.
- ≤1 metastatic lesion(s) for lifileucel generation and ≤1 remaining measurable lesion as defined by RECIST v1.1.
- Adequate organ function.
- Patients of childbearing potential or those with partners of childbearing potential must be willing to practice an approved method of highly effective birth control.

**Exclusion Criteria**

- Melanoma of uveal/ciliary origin.
- Symptomatic untreated brain metastases.
- Prior therapy for metastatic disease >1 prior line of therapy.
- Patients with a BRAF/VEGFD mutation-positive tumor who received prior adjuvant/ neoadjuvant IC1 therapy only.
- Active medical illnesses (eg, systemic infections; seizure disorders; coagulation disorders; other active major medical illnesses of the central nervous system, respiratory, or immune systems).
- Any form of primary or acquired immunodeficiency (eg, SCID, AKD).
- Other primary malignancy in the last 3 years.
- Allergic or autoimmune disorder.

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**References**

- Li Y, et al. Submitted for publication.

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**Disclosures**

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