Contemporary Real-World Patient Characteristics, Treatment Patterns, and Clinical Outcomes in Metastatic Uveal Melanoma in the United States

ISPOR Acceptance Code: CO16

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Key Takeaways

- **Real-World mUM Cohort:** Evaluated real-world treatment patterns and risk-set adjusted (RSA) real-world overall survival (rwOS) in a US cohort of adults with metastatic uveal melanoma (mUM) across community (50.7%) and academic settings.
- **Heterogeneous Treatment Landscape:** Usage spans multiple therapeutic classes (ipilimumab + nivolumab, LDTs ± systemic therapy, tebentafusp, and others) with frequent regimen switches and sequencing across treatment episodes.
- **High Unmet Need:** Real-world survival in mUM remains poor (overall median rwOS: 8.7 months from 1st treatment), demonstrating a high unmet need across current standards of care.

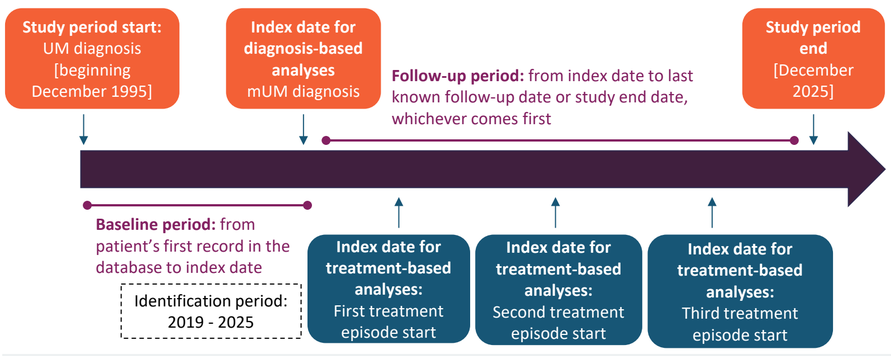
Introduction

- Uveal melanoma (UM) is a rare disease but the most common adult intraocular malignancy
- Up to 50% of patients with UM ultimately develop metastatic disease, most commonly involving the liver
  - Prognosis after metastatic diagnosis remains poor due to limited treatment options in mUM
- The only FDA-approved systemic treatment for mUM is tebentafusp, however it is limited to HLA-A*02:01-positive patients
- This study described patient characteristics, treatment patterns, and real-world outcomes among US patients with mUM

Methods

This retrospective observational study used the Tempus AI database and included adults diagnosed with mUM from 2019-2025. The index date was the first documented mUM diagnosis for patient characteristics and diagnosis-based rwOS, and treatment initiation for treatment patterns, real-world time to next treatment (rwTTNT), real-world time on treatment (rwTOT), real-world progression free survival (rwPFS), real-world best overall response (rwBOR), and treatment-based rwOS. Systemic, localized, and liver directed therapies (LDTs) initiated after mUM diagnosis were evaluated to identify the first three treatment episodes.[1] Time-to-event outcomes were estimated using RSA Kaplan-Meier methods with two-sided 95% confidence intervals (CI).[2]

Figure 1. Study Design Schematic



Criteria

- Documented primary diagnosis of UM
- Aged ≥ 18 and ≤ 89 years at primary diagnosis
- Received genomic sequencing via a Tempus-based tissue assay
- Documented mUM between 2019 and 2025
- No non-uveal primary melanoma diagnosis within 5 years of metastasis date (exclusion)

[1] Treatment episodes were defined based on treatment type and timing: LDTs and systemic therapies initiated within 30 days were classified as a single treatment episode, whereas therapies following disease progression, regimen switches, or extended gaps (>30 days for LDTs) were classified as distinct treatment episodes. Maintenance nivolumab was categorized within the primary systemic treatment episode. [2] LDTs represent non-systemic/localized therapies and included hepatic infusion (isolated, percutaneous, or hepatic arterial), embolization (chemoembolization, radioembolization, or immunoembolization), ablation (thermal, percutaneous, or cryotherapy), surgical procedures (resection and enucleation), and radiotherapy (brachytherapy, stereotactic, or external beam). [3] Patients are not observable in the Tempus multimodal database until they are sequenced, which can occur after mUM diagnosis or first treatment (i.e., "delayed entry"). This creates immortal time bias as patients must survive long enough to be sequenced. RSA accounts for delayed entry by only counting a patient in the risk-set from the latter of index date or sequencing date. Outcome time is still measured from the index date. Patients who experienced the outcome prior to sequencing are excluded, as patients cannot contribute to survival estimates before entering the study.

Results

- Among 160 (73.1%) patients with documented treatment during the study period, ipilimumab + nivolumab was the most common 1st treatment (n=72, 45.0%), followed by LDTs ± systemic therapy (n=44, 27.5%) and tebentafusp (n=18, 11.3%), with other therapies comprising the remaining 16.3% (n=26)[4]
- Median rwTTNT and rwTOT from 1st treatment were 3.8 months (95% CI: 2.5-5.6) and 2.5 months (95% CI: 2.1-3.2), respectively
- From mUM diagnosis, median rwOS was 9.2 months (95% CI: 6.0-11.4). From 1st treatment, median rwOS was 8.7 months (95% CI: 6.0 - 11.4), but varied by treatment class: 17.0 months (95% CI: 4.6 - 30.9) for tebentafusp, 13.3 months (95% CI: 7.4 - 21.9) for LDTs ± systemic therapy, and 5.95 months (95% CI: 2.7 - 11.0) for ipilimumab + nivolumab
- From 1st treatment, median rwPFS was 2.6 months (95% CI 1.7 - 3.6)[5]
- Physician-documented responses were not routinely captured for all patients, with no patients demonstrating complete response. Among the 51 documented patients, 4 had partial response, 12 had stable disease, and 35 had progressive disease[6]

Table 1. Patient Characteristics

Characteristic	Overall (N=219)*
Age at metastatic diagnosis, years	
Median [IQR]	65.0 [57.5 - 72.0]
Sex, n (%)	
Female	115 (52.5%)
Male	104 (47.5%)
Race, n (%)	
White	155 (93.4%)
Black or African American	0 (0.0%)
Asian or Other Race	11 (6.6%)
Not documented	53
Region, n (%)	
Midwest	102 (49.3%)
West	51 (24.6%)
South	46 (22.2%)
Northeast	8 (3.9%)
Not documented	12
Institution type, n (%)	
Academic Only	84 (38.4%)
Community Only	111 (50.7%)
Both	24 (11.0%)
Metastatic site, n (%)	
Liver Only	147 (67.1%)
Extrahepatic Only	28 (12.8%)
Both	44 (20.1%)
HLA-A*02:01 status, n (%)**	
Positive	96 (50.5%)
Negative	94 (49.5%)
Not documented	29
Time from primary UM diagnosis to metastases, years	
Median [IQR]	3.1 [1.5 - 6.4]

*Percentages include patients with known/documented values only.
**HLA-A*02:01 status was defined using all available biomarker data from time of primary UM diagnosis through the end of the study period, as HLA-A*02:01 status is not expected to change.

Table 2. rwBOR from First Treatment Episode

Best Overall Response	Overall (N=106)*
Complete Response	0 (0.0%)
Partial Response	4 (7.8%)
Stable Disease	12 (23.5%)
Progressive Disease	35 (68.6%)
Not documented	55

*Excludes patients whose first treatment episode was sourced from claims data (n=54), as response data was not captured in claims. Percentages include patients with known/documented values only.

Figure 2. Overall rwOS from mUM Diagnosis

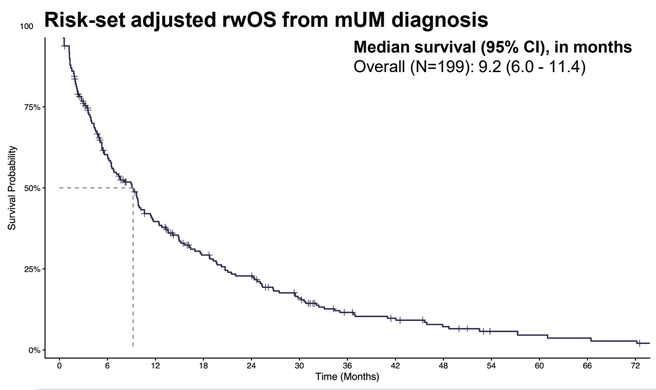


Figure 3. rwOS from First Treatment Episode by Treatment Class[8]

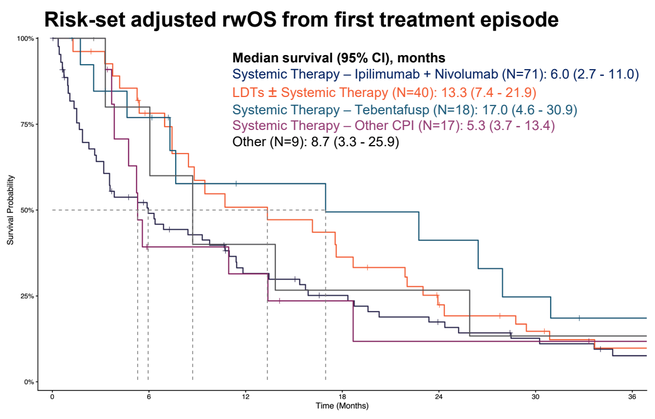


Figure 4. Overall rwPFS from First Treatment Episode[9]

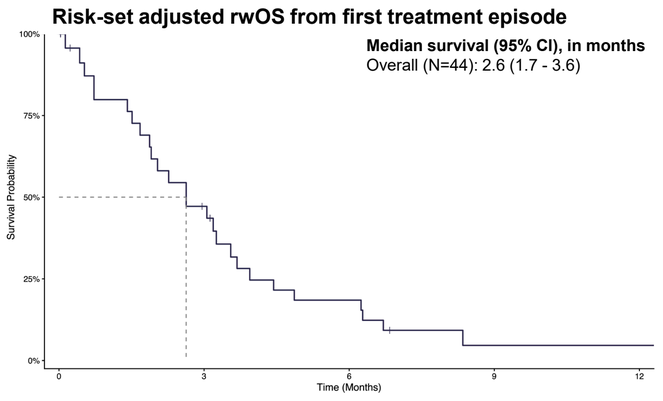


Figure 5. Distribution of First Treatment Episode Classes by mUM Diagnosis Year[7]

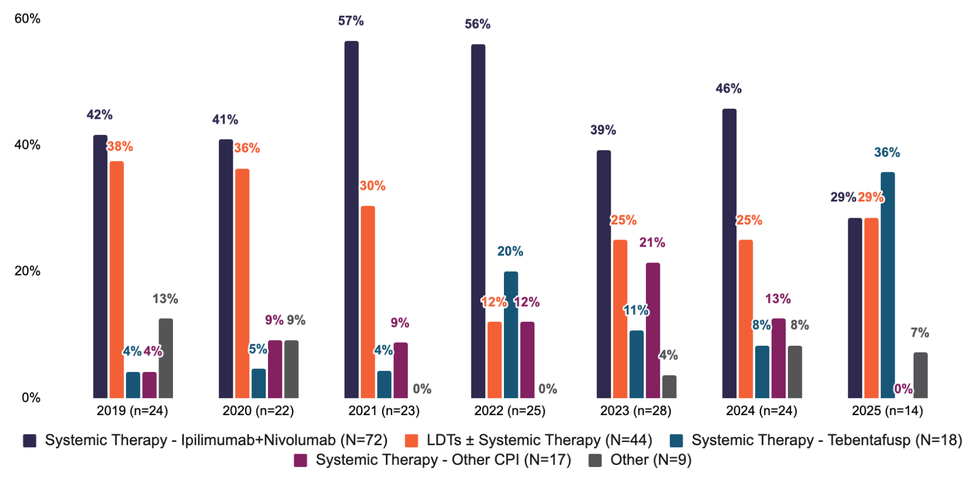
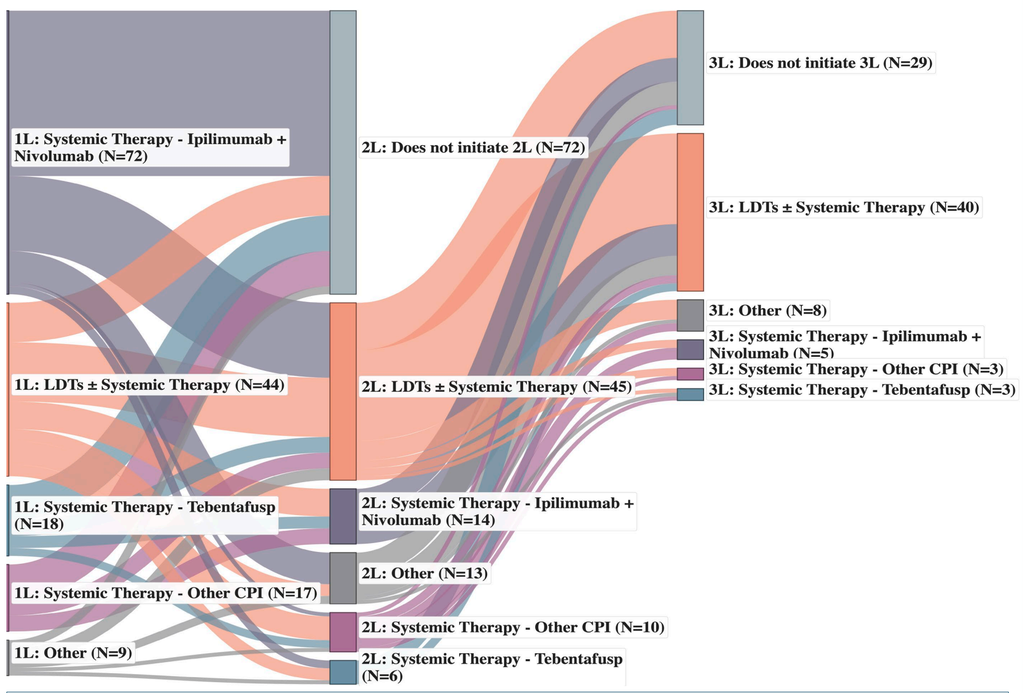


Figure 6. Real-World Treatment Sequencing Across Treatment Episodes



[4]Other therapies include single-agent checkpoint inhibitors (CPI), non-ipilimumab+nivolumab CPI combinations, targeted therapies, chemotherapy, and investigational therapies. [5]Patients whose 1L was derived from claims data (n=54) were not included in the analysis of rwPFS or rwBOR, as progression data and response assessments are not captured in claims data. [6]Responses were attributed to a treatment if they occurred after treatment initiation and on or before initiation of a subsequent treatment or loss to follow-up. [7]Two patients received tebentafusp prior to regulatory approval, due to expanded access programs or clinical trial participation; One patient initiated a tebentafusp-containing treatment episode prior to regulatory approval, with tebentafusp added post-approval. [8]Follow-up is truncated at 36 months for display as fewer than 10 patients remained at risk beyond this point. All available follow-up was included in the estimation of rwOS. [9]Follow-up is truncated at 12 months for display as fewer than 10 patients remained at risk beyond this point. All available follow-up was included in the estimation of rwPFS.

Conclusions

- **Varied treatment sequencing:** Ipilimumab+nivolumab was the most commonly documented first treatment, followed by LDTs with or without systemic therapy and tebentafusp. Subsequent treatment episode patterns varied and included increasing use of localized approaches in later episodes, reflecting heterogeneous real-world management.
- **Limited treatment effectiveness:** Treatment changes occurred within relatively short intervals and best overall response from first treatment was limited, suggesting limited treatment effectiveness in observed care.
- **Poor outcomes underscore continued unmet need:** Survival after metastatic diagnosis and first treatment episode remain limited in this real-world cohort. Additionally, a substantial proportion of patients were HLA-A*02:01-negative and ineligible for tebentafusp, highlighting the need for new treatment options with improved effectiveness.

Limitations

- As a non-interventional, retrospective, and descriptive analysis, this study is subject to limitations inherent to observational real-world data, including residual confounding, unmeasured covariates, and treatment-selection bias. Residual unmeasured clinical heterogeneity and evolving practice patterns across the multi-year study period (pre-2022 and post-2022 eras) may contribute to survival differences relative to trial cohorts.
- The cohort used for this study consists of patients who were sequenced at Tempus and treated in the US. Generalizability to all mUM patients in the US requires further investigation.
- Approximately one-quarter of patients (26.9%) did not have documented treatment during the study period, which likely reflects data capture limitations rather than true non-treatment. Specifically, treatment received as part of clinical trials may be incompletely captured in EHR and claims data. Because mUM patients may receive investigational therapies, this could lead to under-ascertainment of treatment exposure.
- The cohort was predominantly community-based and had limited representation of patients treated in the Northeast, including at centers specializing in mUM trials. Care at these centers may be incompletely captured, limiting generalizability to academic and clinical trial populations.

Abbreviations: UM: uveal melanoma; mUM: metastatic uveal melanoma; rwOS: real-world overall survival; rwTTNT: real-world time to next treatment; rwTOT: real-world time on treatment; rwPFS: real-world progression free survival; rwBOR: real-world best overall response; CI: confidence intervals; LDTs: liver directed therapies; NGS: next-generation sequencing; IQR: interquartile range; HLA: human leukocyte antigen; rwBOR: real-world best overall response

References: Ziogas DC, et al. Curr Oncol Rep. 2025;27:803-21. Jochems A, et al. Cancers. 2019;11:1007. Jager MJ, et al. Nat Rev Dis Primers. 2020;6:24. On S, et al. Cancers. 2026;18:394.