Lumanity

Treatment Pattern of Uveal Melanoma: A Systematic Review

Authors: Rishabh Verma, Sumi Pillai, Vyshnavi Telukuntla, Inderpreet Khurana, Amit Ahuja

Affiliations: Lumanity, Gurugram, India

INTRODUCTION

- Uveal melanoma, the most prevalent primary intraocular cancer in adults, is known for its aggressive behaviour and high likelihood of metastasizing, particularly to the liver[1]
- Uveal melanoma originates either from the ciliary body, iris, or choroid. It has significant consequences, including vision loss and a 15-year disease-specific mortality rate of 45%[2]
- In recent years, the treatment landscape for this condition has undergone substantial changes, with significant advancements in both local and systemic therapeutic options

OBJECTIVES

- This systematic literature review aims to evaluate real-world treatment strategies employed for adult patients diagnosed with uveal melanoma, as well as to assess their adherence to clinical practice guidelines

METHODS

- A systematic search was conducted using the Embase® and MEDLINE® databases via Embase.com to identify English-language articles published after 2010 that report real-world treatment patterns for adults with uveal melanoma. In addition, clinical practice guidelines (CPGs) were sourced from grey literature searches
- All the records retrieved from the literature search were screened per the pre-defined inclusion criteria (Table 1), first based on the title and abstract and then on the full-text citations
- The eligibility of publications was assessed by two independent reviewers, with any discrepancy resolved by a third

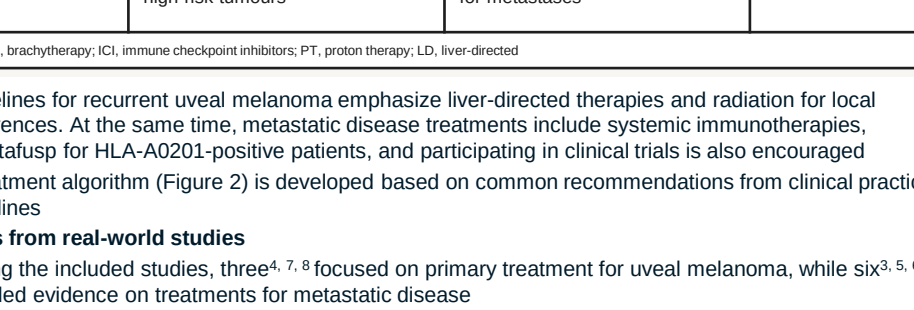
Table 1. Study eligibility criteria

Population	Adult patients with uveal melanoma (including metastatic disease)
Language	English
Time frame	2010–2024
Outcomes	Treatment pattern and treatment recommendation (from guidelines)
Intervention and comparator	No restrictions

RESULTS

- A total of 1,032 records were screened using predefined Population, Intervention, Comparison, Outcomes, and Study-based criteria; nine studies[3-11] were identified and are included in this review
- Five CGPs[12-16] were identified through grey literature searches. Two guidelines were from the USA, and one each were from Europe, Canada, and the UK (Figure 1)

Figure 1. Study flow diagram



Key: CPG, clinical practice guideline.

Findings from clinical practice guidelines

- Overall, the five guidelines for uveal melanoma treatment show consistent recommendations for primary treatment, with options like brachytherapy, proton beam therapy, and enucleation depending on tumour size, location, and patient symptoms. Recommendations are summarised in Table 2

Table 1. Summary of treatment recommendation across clinical practice guidelines

Guideline	Primary treatment	Secondary treatment	Advanced disease
UK National Guidelines[12]	BT for tumour ≤ 8mm, PT for medium tumour and enucleation for large	Radiation-recurrence, LD treatments, surgical resection for select patients	ICI, LD for metastasis, Prognostication
National Comprehensive Cancer Network (NCCN)[13]	Observation for small tumours, BT for tumours ≤ 10 mm, PT near sensitive structures, enucleation for large or symptomatic tumours	Radiation for recurrent disease, LD therapies for metastases	ICI, combination for metastasis, LD for hepatic
European Association of Dermato-Oncology[14]	PT, BT, or enucleation based on tumour size/location, early treatment for small, high-risk tumours to prevent progression	Surgery for local recurrences, LD therapies, radiation for unresectable cases	Tebentafusp for HLA-A*0201+, LD, combination
American Society Of Clinical Oncology[15]	Enucleation, BT for localized tumours, PT for medium-to-large tumours	Radiation for recurrence, liver interventions, regular surveillance	Anti PD-1, combo therapy, trials
Cancer Care Alberta[16]	BT for small/medium tumours, PT for large tumours, enucleation for high-risk tumours	Radiotherapy/laser-recurrences, Surgical re-excision – local, LD for metastases	PD-1 inhibitors, trials, LD for metastasis

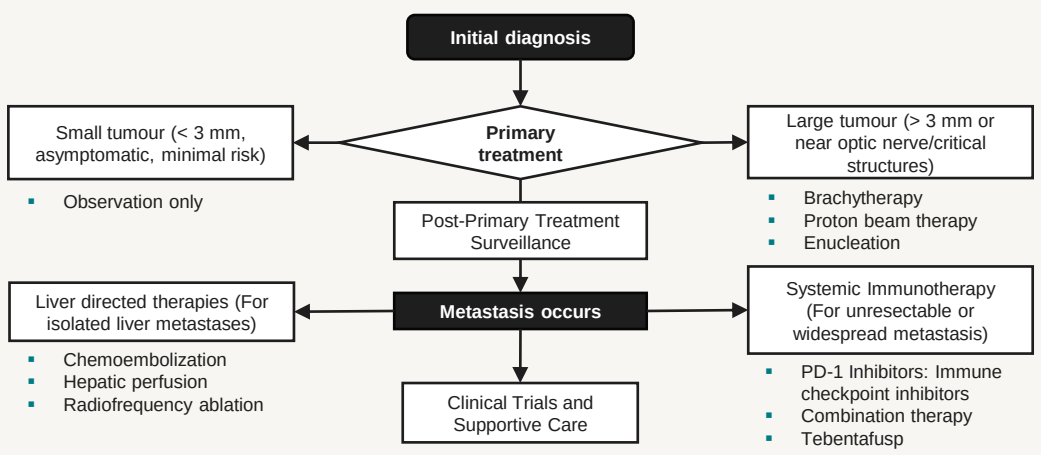
Keys: BT, brachytherapy; ICI, immune checkpoint inhibitors; PT, proton therapy; LD, liver-directed

- Guidelines for recurrent uveal melanoma emphasize liver-directed therapies and radiation for local recurrences. At the same time, metastatic disease treatments include systemic immunotherapies, tebentafusp for HLA-A0201-positive patients, and participating in clinical trials is also encouraged
- A treatment algorithm (Figure 2) is developed based on common recommendations from clinical practice guidelines

Findings from real-world studies

- Among the included studies, three[4, 7, 8] focused on primary treatment for uveal melanoma, while six[3, 5, 6, 9-11] provided evidence on treatments for metastatic disease
- These studies were conducted across various geographies like Australia, Belgium, Canada, Germany, India, Italy, Netherlands, and USA

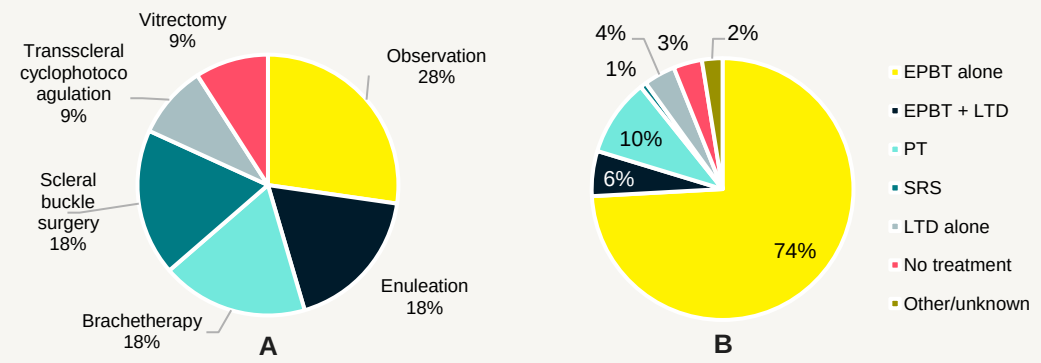
Figure 2. Treatment algorithm based on clinical practice guidelines



Initial treatment of Uveal melanoma

- Wong et al.[4] reported that, after the initial diagnosis of Uveal melanoma, 28% of patients were kept under observation, 18% received brachytherapy and 18% received enucleation. Other treatments were also administered, as presented in Figure 3A
- The Chevli et al. study[7] queried the National Cancer Database (NCDB) from 2004–2015. It was reported that 20% (n = 3,167) of patients received enucleation and 80% (n = 12,495) received globe-preserving modalities, as presented in Figure 3B. The authors also reported, that in a large tumour cohort, the EPBT rate increased from 30% in 2004 to 45% in 2015, while the enucleation rate remained largely unchanged

Figure 3. A) Primary treatment of uveal melanoma[4] B) Globe preserving modality[7]

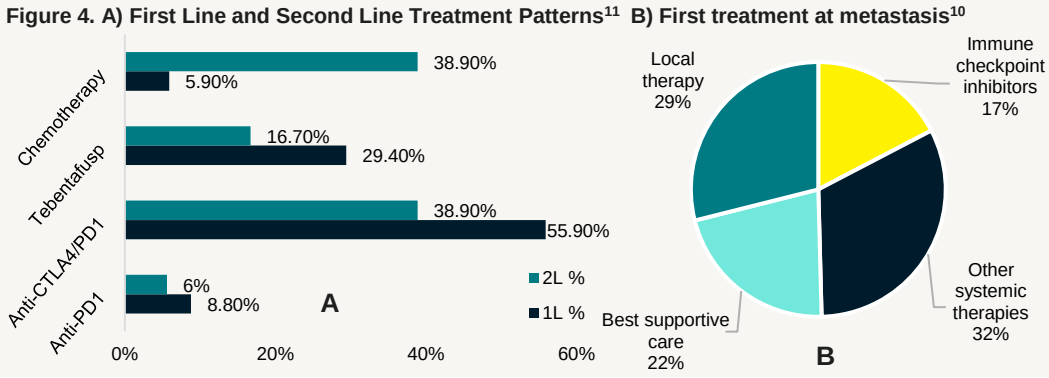


Key: EPBT, eye plaque brachytherapy; LTD, local tumour destruction; PT, proton therapy; SRS, stereotactic radiosurgery

Treatment of metastatic uveal melanoma

- Treatment of metastatic disease included systemic therapies like immune checkpoint inhibitors (ICIs), chemotherapies, and tebentafusp
- Staeger et al.[11] reported that first and second-line systemic treatment for metastatic uveal melanoma included anti-PD1, anti-CTLA4, tebentafusp, and chemotherapy. Anti-CTLA4 combination was the most utilized first-line treatment (55.9%), indicating a significant trend towards first-line immunotherapy (Figure 4A)
- Vanaken et al.[10] reported that initial treatments for patients with metastatic disease included ICIs, local therapies such as liver-directed treatments and liver surgery, and best supportive care. Additionally, patients received other systemic therapies, including dacarbazine, cisplatin, fotemustine, carboplatin-paclitaxel, and temozolomide. Figure 4B presents the proportion of patients receiving different treatments

Figure 4. A) First Line and Second Line Treatment Patterns[11] B) First treatment at metastasis[10]



- Steeb et al.[6] reported various systemic therapies that were given in metastatic disease, including nivolumab + ipilimumab (80%), nivolumab (50%), pembrolizumab (40%), MEK inhibitors (35%), and ipilimumab monotherapy (15%)

CONCLUSIONS

- Evidence indicates a growing preference for globe-preserving approaches, particularly EPBT, over enucleation for tumour management
- The review highlights a significant shift towards immunotherapy, with Anti-CTLA4 combination and tebentafusp emerging as key first-line treatments for metastatic uveal melanoma
- The findings from the real-world studies were consistent with the global clinical practice guidelines

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