An Integrated Liquid Biopsy Analysis for Comprehensive Investigation of Uveal Melanoma

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Introduction

- Uveal melanoma (UM) is the most common primary intraocular tumor in adults and accounts for <5% of all melanomas.
- Approximately 50% of patients with early-stage UM will develop metastatic disease.
- There are no blood biomarkers currently that identify patients with the UM who are at higher risk of disease relapse.
- It is hypothesized that the presence of circulating tumor cells (CTCs) and cell-free DNA (cfDNA) prognosticate an increased risk of relapse.

Objective

- Determine factors associated with survival for early-stage and metastatic UM patients.
- Identify biomarkers (CTCs, cfDNA, circulating tumor DNA (ctDNA)) associated with relapse.

Methods

- **Review of data on patients:**
  - Presenting at MD Anderson with UM from 12/1/2014 to 7/26/2023
  - Enrolled in IRB Protocol LAB11-0314
- **Factors examined:**
  - Patient demographics
  - Clinicopathologic features
  - Treatment strategies
- **Biomarkers obtained from peripheral blood samples:**
  - CTCs using the CellSearch Circulating Melanoma Cell Assay®
  - cfDNA using MagMax™ cell-free DNA Isolation Kit, Oncomine™ Pan-Cancer Assay, and Ion Torrent™ Technology
- **Statistical analyses:**
  - Unpaired t-test, univariable and multivariable Cox regression modeling

Longitudinal Blood Biopsy Timeline

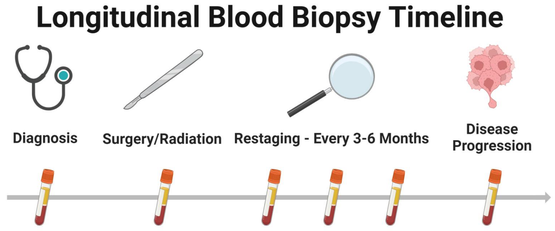

Figure 1. Liquid biopsy collection time points for patients with uveal melanoma.

Acknowledgments

Thank you Lucci Lab for advancing my understanding of clinical science and magnifying my interest in ophthalmic and surgical oncology.

Utilizing Liquid Biopsies for Prognostication and Disease Monitoring in Uveal Melanoma

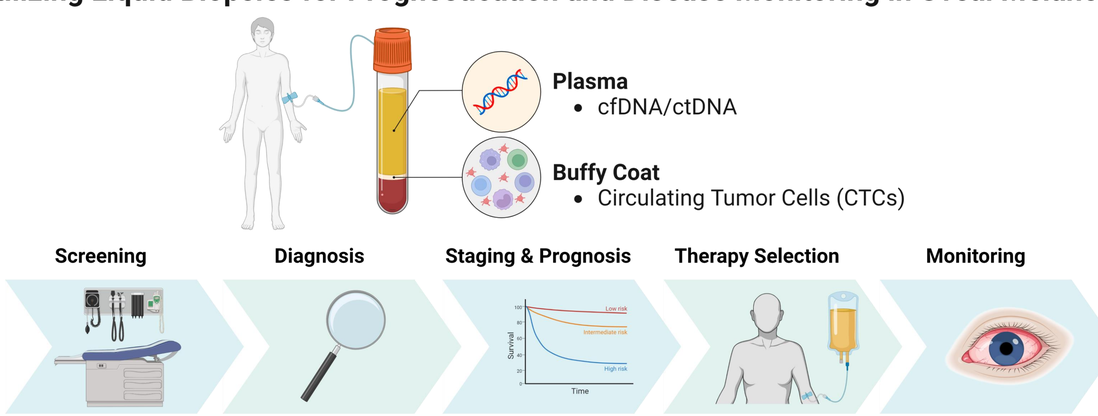

Figure 2. Application of a liquid biopsy approach for cancer treatment and surveillance.

Results

Total Patients (n = 157)	
Sex	
Male	72 (46%)
Female	85 (54%)
Median age at diagnosis	55 years (19-83 years)
Ethnicity	
Non-Hispanic	147 (94%)
Hispanic or Latino	4 (2%)
Unknown	6 (4%)
Disease status at study enrollment	
Early-stage disease	111 (71%)
Metastatic	46 (29%)
Classification	
Class 1A	25 (16%)
Class 1B	16 (10%)
Class 2	55 (35%)
Unknown	61 (39%)
PRAME	
Positive	25 (16%)
Negative	44 (28%)
Unknown	88 (56%)
Tumor mutation analysis (*n = 53*)	
Wildtype	2 (4%)
GNAQ	28 (53%)
BAP1	16 (30%)
GNA11	20 (38%)
Other	16 (30%)
Median time between diagnosis and first blood sampling	21.42 months
Early-stage	10.58 months
Metastatic	26.08 months
Total Study follow-up	63.83 months
Early-stage	74.25 months
Metastatic	33.54 months

Table 1. Patient characteristics.

ctDNA	Tumor Panel	Concordance	Days Difference
MAP2K1	GNAQ, TP53	NO	975
GNA11	GNA11	YES	944
GNAQ, MAP2K1	GNAQ	YES	358
MAP2K1, GNAQ	GNAQ	YES	9
RAF1, EGFR,MAP2K1	GNAQ	NO	1072
GNAQ, MAP2K1, TP53	GNAQ	YES	400
GNAQ	GNAQ	YES	237

Table 2. (above) cfDNA mutations compared to mutations in the tumor tissue.

Variables	HR	*p*	95% CI	
≥1CTC	0.38	0.06	0.14	1.03
Relapse	0.52	0.05	0.27	1.01
BMI	0.06	0.06	0.02	1.11
Melanoma Specific Death	0.60	0.15	0.31	1.20
CMC(Positive/Negative)	0.61	0.15	0.31	1.20
Disease Stage (AJCC 8th)	0.62	0.17	0.31	1.23
Gender	0.67	0.26	0.34	1.34
Immunotherapy	0.73	0.35	0.37	1.42

Table 3. (above) Univariate Cox Regression Analysis of Relapse Free Survival Associated with CTC Detection in Overall Cohort at Draw 1.

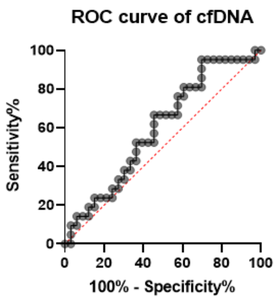

Figure 3. (left) Based on relapse and non-relapse patient data, an ROC curve was plotted to determine the Area Under the Curve (AUC) and a cfDNA cut-off value for a positive cfDNA result was >3.9 ng/mL.

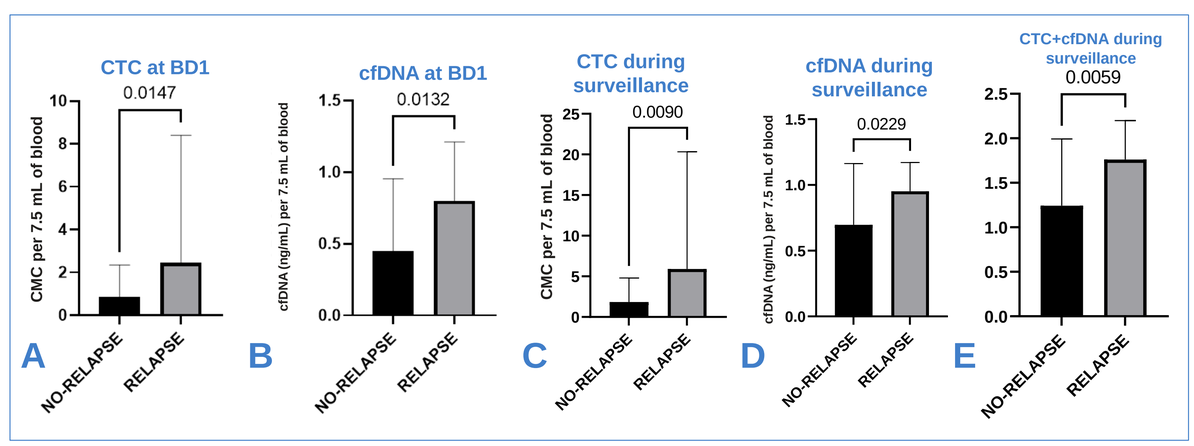

Figure 4. Association between relapse and: **(A)** CTC at first blood draw (BD1). **(B)** cfDNA at first blood draw (BD1). **(C)** CTC during disease monitoring. **(D)** cfDNA during disease monitoring. **(E)** CTC and cfDNA during disease monitoring.

Case Studies

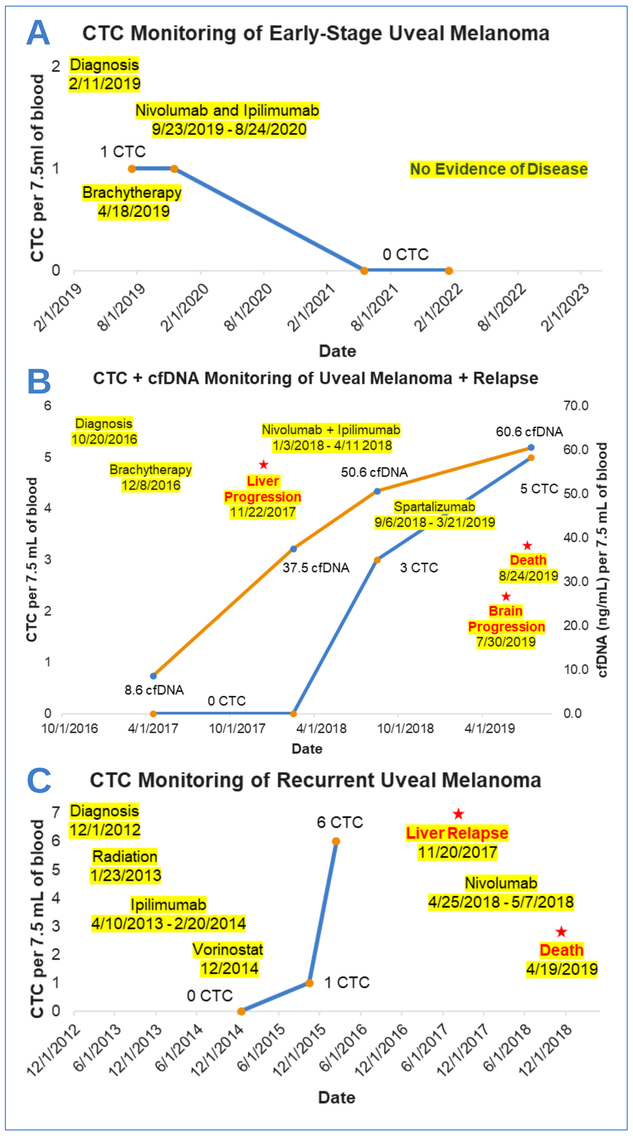

Figure 4. Liquid biopsy offers clinical utility for monitoring UM patients: before, during, and after **(A)** immunotherapy and **(B)** treatment to monitor response. **(C)** during active surveillance to monitor disease recurrence.

Conclusions

- Patients with UM and a positive liquid biopsy (≥1 CTC and cfDNA >3.9 ng/mL) during surveillance are more likely to relapse than patients with a negative liquid biopsy.
- A comprehensive liquid biopsy approach has the potential to offer risk stratification as well as non-invasive disease monitoring clinical utility.

Future Studies

- Examine extracellular vesicles and circulating miRNAs influence on UM prognosis and relapse.
- Conduct a prospective study involving patients presenting with UM and received treatment at MDACC to study the prognostic and predictive value of liquid biopsy.

References

Anand K *et al*. *Cancers*. 2019; 11(6):856
Chattopadhyay, C *et al*. *Cancer*. 2016; 122(15):2299-312