Case Studies & Publications

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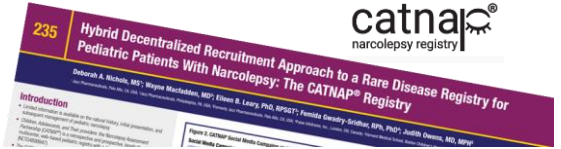
Publications demonstrate RWD impact / use cases

Pulse engages registry sponsors and partners with Scientific Advisory Board members to collaborate on abstracts and posters and has supported numerous publications at major conferences with insights that inform treatment and reimbursement decisions, treatment sequencing, and the impact of decentralized and hybrid study designs.

200+ team publications: https://www.pulseinfoframe.com/papers-publications/

Shows the rapid study startup process in collaboration with advocacy.

Shows that real-world data provide critical context to clinical trials and inform treatment and reimbursement decisions.



Shows the impact of accelerated enrollment through hybrid study design with decentralized arm.

CDKL5

Case Studies & Publications

CDKL5 Global Registry

Key statistics

2 PARTNERS

The **CDLK5 Registry** was created in 2018 in collaboration with the LouLou Foundation and Orphan Disease Center (UPenn).

loulou FOUNDATION

the orphan disease center

GROWTH

GUID leveraged to support additional observational studies, including an endpoint-enabling study launched in 2021 with a pre-competitive pharma consortium.

ultragenyx · Amicus Therapeutics · loulou FOUNDATION · ELAAJ BIO · Biogen · PTC THERAPEUTICS · MARINUS PHARMACEUTICALS · ZOGENIX

PUBLICATIONS

Data from the **CDLK5 Registry** has been used in publications to increase the understanding of the disease.

PATIENTS ENROLLED

Since its launch, the **CDLK5 registry** has enrolled over 170 patients and the number of anticipated patients is ~300.

Global Access

The **CDLK5 Registry** has enrolled patients around the world, with the largest dataset collected on the CDLK5 community coming from the US and data shared with Australian researchers through our GUID.

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Timeline

2016

Collaboration formed with the LouLou Foundation and Orphan Disease Center (UPenn)

2018

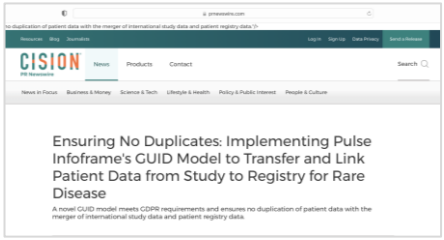
The **CDLK5 Registry** is launched, powered by Pulse's platform

2021

Pre-competitive pharma consortium established to initiate an endpoint-enabling study: CANDID

2022

Pulse GUID implemented to link CDKL5 Registry and CANDID Study data



2024-

Registry infrastructure and GUID leveraged to support additional observational studies

CDKL5 Global Registry

Goals, Impact, and Vision

WHAT?

A significant gap in the assessment of patient treatment and outcomes because of the lack of systematically captured, reported or analyzed Natural History of Disease.

WHY?

Physicians lacked insights on:

- Survivorship
- Quality of life (patient and caregiver)
- Lifetime cost of treatment
- Social impact of treatment
- Disease progression

HOW?

The CDKL5 Registry collects information from family/caregivers that links to clinical data.

Families are fully consented to learn about opportunities for CDKL5 clinical studies.

Pulse Infoframe provides a secure, data privacy-compliant, centralized evidence generation platform which meets regulatory requirements for clinical data.

RESULTS

Capturing Natural History of Disease data has led to a deeper understanding of:

- Implications and impact of genotyping
- Quality of life
- Impact of reduced time-to-diagnosis
- Guidance for symptom management
- Patient and caregiver preferences
- Implications for large patient cohorts and population health

Incredible value for industry, physicians, payers, and most importantly patients has been unlocked, including::

- Greater number of companies being involved in drug development
- Endpoint-enabling study
- An MOU was established by Pulse to link data between the CDKL5 ODC registry and the IFCR funded Australian work
- What's next ? Additional studies and forming a central repository for CDKL5 data

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Uveal Melanoma

Case Studies & Publications

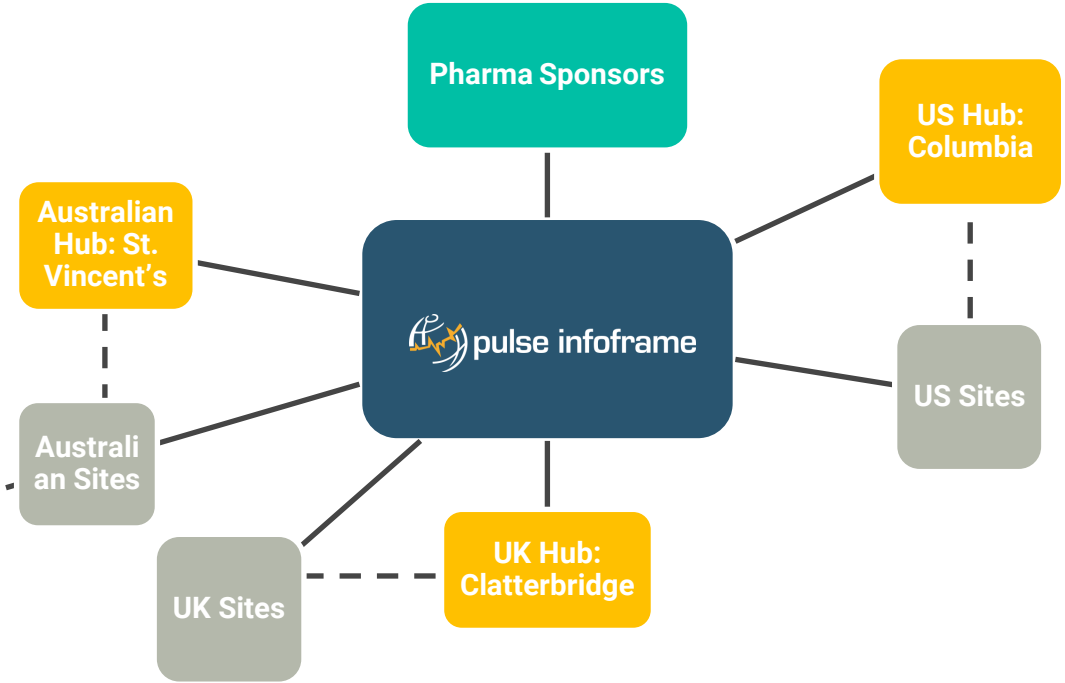
Case Study: The Uveal Melanoma registry

The Uveal Melanoma registry was launched in March 2020 with the support from Immunocore, after a development phase that began in 2018.

During its development, the scope and size of the registry changed significantly, although it was still possible for Pulse to deliver a platform that collects 360+ data elements that are based on PI's guidance and it is inclusive of retrospective and prospective data

The expanded variables within the platform include tumor characteristics, systemic therapies, biomarkers, biobanking, distant metastasis and treatment, ECOG status, surveillance, comorbidity and others.

Initially launched in 11 sites across the US, UK, Canada and Australia, this has now increased. The registry utilizes a hub and spoke model where the Pulse platform is set up to ingest data from multiple sites in multiple countries. The platform has been developed to support current plans to expand the registry into new countries and to establish new sites in the original countries through additional sponsorship.



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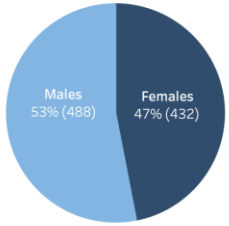
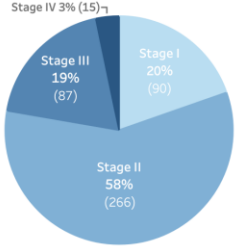
Uveal Melanoma Registry

Uveal Registry Participants
N=920
(Wednesday, February 21, 2024)

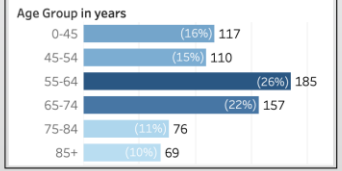
Patient Sex



Stage at Diagnosis



Age at Diagnosis

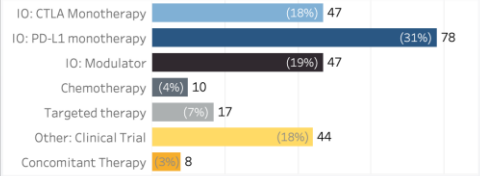


North America
N = 542

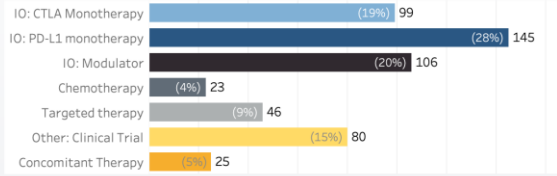
United Kingdom
N = 86

Australia
N = 292

Participant 1st Line-of-Therapy Frequency

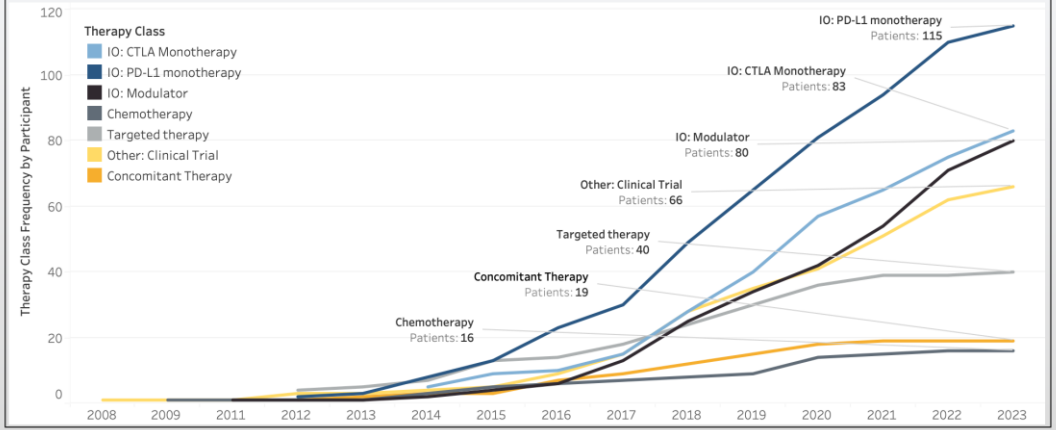


Cumulative Total of all Therapy Exposures



Cumulative Total of Drug Therapy Class Use by Participants (by year)

(*Participant may contribute to more than 1 therapy class.)



Capturing uveal melanoma (UM) global practice patterns and clinical outcomes in the collaborative ocular melanoma natural history (OMNi) study (NCT04588662)

Joseph J. Sacco, Marlana M. Orloff, Sapna Pradyuman Patel, Max Conway, Li-Anne Lim, Lotte S. Fog, David Sia, John McKenzie, Daniel McKay, Roderick O'day, Timothy Isaacs, Alexander Noor Shoushtari, Ryan J. Sullivan, Sarah Kin, Femida Hussein Gwadry-Sridhar, Anthony M. Joshua, Richard D. Carvajal

The OMNi dataset can serve and aid in interpretation of clinical trial outcomes in the real-world, facilitate cutting-edge research, and accelerate the development of diagnostics and therapeutics.

Summary:

- **An ambispective database developed to provide contemporary real-world data of UM, capturing its natural history and serving as a virtual biospecimen repository**
- **Objective to characterize regional/international UM management practice patterns and associated clinical outcomes to inform best practice recommendations.**
- **Will facilitate new insights, hypothesis testing, as well as clinical trial development and conduct**
- **Governance structure to make accessible for research**

Pulse manages the OMNi registry – co-designed program, hosted on healthie® platform, manages sites, data curation, and is responsible for commercial relationships with biopharma

- Large registries providing robust cohorts for sub-analysis (e.g., specific mutations)
- Diverse populations including under-represented groups across multiple sites
- Uniform data and disease models, and curation across sites and conditions

Adjuvant Crizotinib in High-Risk Uveal Melanoma Following Definitive Therapy

Shaheer Khan, Jose Lutzky, Alexander Noor Shoushtari, Joanne M. Jeter, Cody Chiuzan, Naomi Sender, Lauren Esther Blumberg, Alexandra Nesson, Shahnaz V. Singh-Kandah, Susana Hernandez, Grazia Ambrosini, Oliver Surriga, Gary K. Schwartz, Richard D. Carvajal

The use of adjuvant crizotinib in patients with high-risk UM did not reduce rates of relapse in this multicenter, single arm trial. 9/32 (28%) pts required dose modification or discontinuation due to AE which may have limited efficacy.

Table 1. Baseline characteristics	
Age at diagnosis (median, range)	60 years (26-86)
Sex	
Male	20 (59%)
Female	14 (41%)
ECOG status (median, range)	0 (0-1)
Race	
White	25 (74%)
Hispanic	2 (6%)
Other/Unknown	7 (20%)
Largest basal diameter (median, range)	14.0 mm (12-21mm)
Ciliary body involvement	
Yes	3 (9%)
No	31 (91%)
Primary treatment modality	
Radioactive plaque	24 (71%)
Surgery	10 (29%)

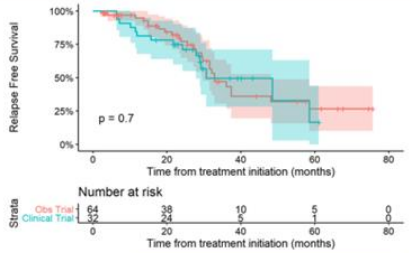


Table 3. Relapse-free survival rates			
	12 mo	24 mo	36 mo
RFS rate	81%	75%	50%
95% CI	68-95%	60-90%	28-71%

OM Ni International Ocular Melanoma Natural History Study

(Khan et al, ASCO 2020)

IRCI International Rare Cancers Initiative Aspiring to improve the lives of patients with rare cancers

Pulse provided the platform, site and data management, and support for this interventional trial within our broader Uveal Melanoma registry

- Existing, established relationships with sites and investigators to facilitate programs
- All data curation and management, investigator dashboards, patient consents and PROs on Pulse Healthie® platform
- Uniform data and disease models, and curation across sites and conditions

Melanoma

GMRN Case Studies & Publications

Global Melanoma Research Network

WHAT WAS THE ISSUE?

The original purpose for the **GMRN registry** when it was developed 10 years ago was to understand how patients are doing after they've received treatments for melanoma. It would address the following:

- What are the benefits?
- What are the outcomes?
- Are there differences based on practice, region, and/or province?

WHY WAS IT NEEDED?

Patients are data generators: they're research partners. Those participating in the **GMRN registry** want to know what the impacts and/or results of the treatments they're undergoing were.

HOW WAS IT DEVELOPED?

The **GMRN registry** makes use of the healthie™ platform which provides a collaborative ecosystem made up of researchers, patients, and industry for drug development increases the chances for developing treatments that truly benefit patients. A platform that supports the voice of the patient while collecting rigorous, regulatory grade data is the solution that can propel research that truly benefits patients.

WHAT ARE THE RESULTS?

Treatments have evolved over the last 10 years, and the **GMRN registry** has provided both the research and medical communities opportunities to ask detailed questions to not only advance treatments but also to improve treatment outcomes for and impact on patients. As the registry expanded, it's been possible to extend the platform to support subtypes of skin cancers, e.g., Merkle cell, squamous cell, and basal cell carcinoma. Researchers can leverage one platform for exploring multiple other malignant diseases.

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GMRN registry

IMPACT OF THE REGISTRY

"Over the past 10 years, the Global Melanoma Research Network team has been able to track the impact on patients and the efficacy of treatment: Is the treatment having a positive impact? How does the RWD compare to the favorable results reported from the clinical trials?"

Dr. Scott Ernst, PI for Global Melanoma Research Network

4,900+ PATIENTS ENROLLED

Since its launch, the **GMRN registry** was enrolled over 4,900 patients and this number continues to increase

2012 LAUNCH

The **GMRN Registry** was launched in 2012 and the London Regional Cancer Program the first site to register patients. The evidence generated from the platform has been leveraged by over 6 pharma companies for prospective and retrospective(longitudinal), HEOR, quality of life and epidemiological studies

PUBLICATIONS

Data from the **GMRN Registry** has been used in more than 6 publications to increase the understanding of the disease and treatment efficacy. Additionally, over two dozen abstract have been published

15 SITES

With 12 sites throughout Canada, the **GMRN Registry** is the largest registry for the disease in the region

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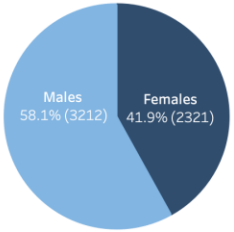
Global Melanoma Registry

Melanoma Registry Participants

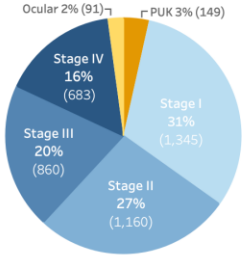
N=5,533

(Wednesday, February 14, 2024)

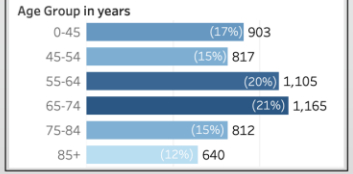
Patient Sex



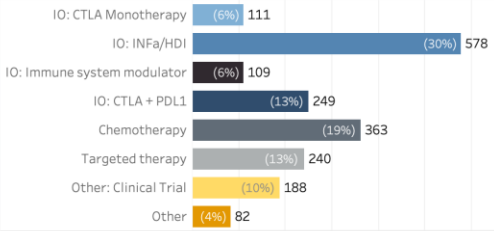
Stage at Diagnosis



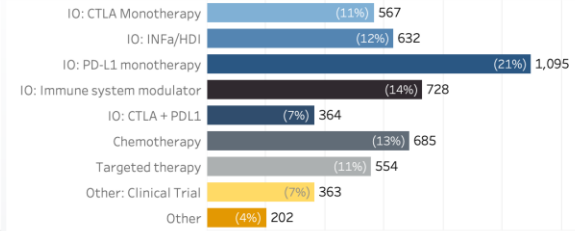
Age at Diagnosis



Participant 1st Line-of-Therapy Frequency

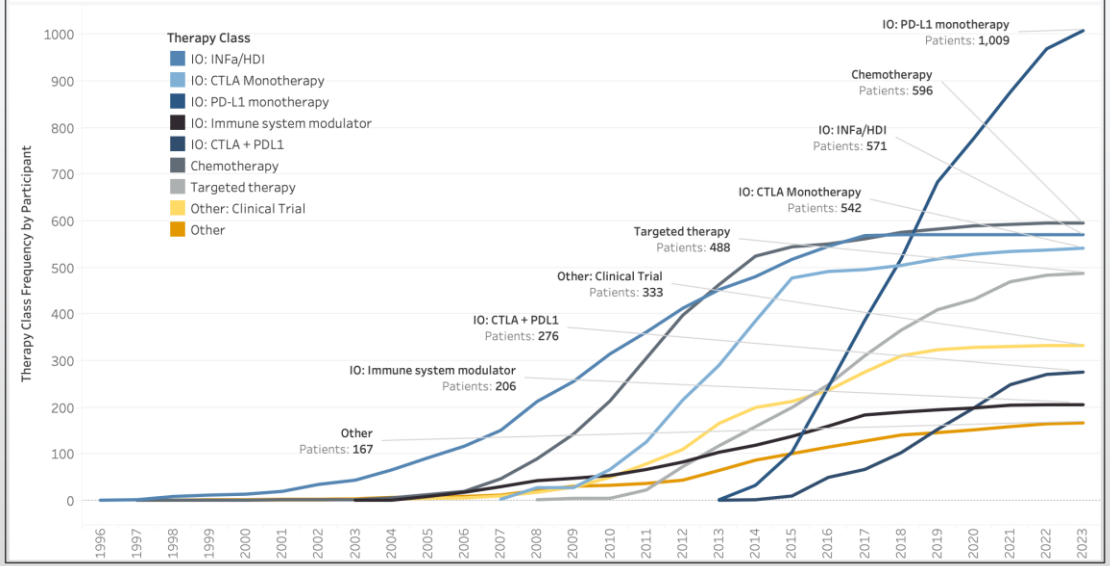


Cumulative Total of all Therapy Exposures



Cumulative Total of Drug Therapy Class Use by Participants (by year)

(*Participant may contribute to more than 1 therapy class.)



Impact of systemic therapy sequencing on overall survival for patients with advanced BRAF-mutated melanoma

Authors: B Adi Kartolo, Jasna Deluce, Wilma M Hopman, Linda Liu, Tara D Baetz, Scott Ernst, John G Lenehan

Division of Medical Oncology, Cancer Care of Southeastern Ontario, Queen's University, Kingston, ON; Division of Medical Oncology, London Regional Cancer Program, London Health Sciences Centre and University of Western Ontario, London, ON; Department of Public Health Sciences, Queen's University, Kingston, ON; Pulse Infoframe, London, ON

Background:

- No clear guideline recommending optimal first-line (1L) therapy in BRAF-mutant melanoma
- Immune checkpoint inhibitor (ICI) vs. BRAF targeted therapy (TT) – does treatment sequencing matter?
- Here, we provide real-world evidence utilizing prospectively collected data from the Canadian Melanoma Research Network (CMRN) database

Methods:

CMRN (9 Cancer Centres in Canada)
Prospective data collection

Inclusion Criteria:
-Unresectable advanced/metastatic cutaneous melanoma
-Targetable BRAF subtypes
-At least 1 cycle of palliative-intent ICI or TT
-At least 1 year follow-up

Exclusion Criteria:
-MEK without BRAF inhibitor
-1L ipilimumab monotherapy

1L ICI
PD-1±CTLA-4 inhibitors with or without subsequent BRAF±MEK inhibitors
(N=80)

1L TT
BRAF±MEK inhibitors with or without subsequent PD-1±CTLA-4 inhibitors
(N=151)

Study Endpoint: Overall Survival (OS) via Kaplan Meier
Multivariable Cox Analysis: ECOG, number of metastasis, brain metastasis, sequencing group

TAKE HOME MESSAGE

Using ICI in first-line shows a trend to improved survival when compared to TT in real-world patients with advanced BRAF-mutant melanoma. 1L-IO patients have a lower chance of requiring second-line therapy due to progression.

MAIN FINDINGS

Figure 1. Overall Survival Based on Treatment Sequence Group

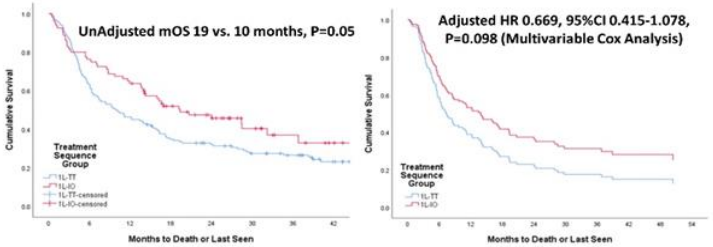


Figure 2. Treatment Sequencing Pattern Based on 1L Regimen

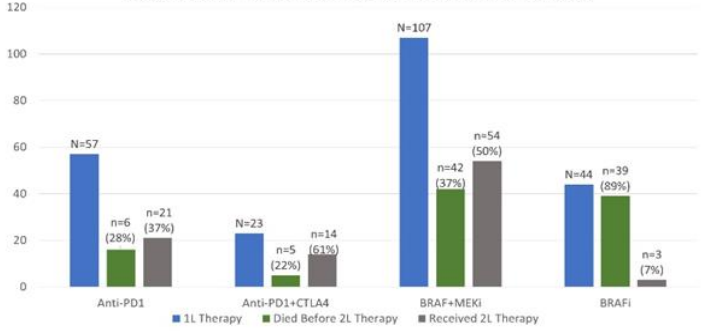


Table 1. Baseline Study Characteristics

	Total (N=231)	1L-ICI Group (N=80)	1L-TT Group (N=151)	P-Value
Age ≥65	118 (51)	44 (55)	74 (49)	0.409
Male Gender	149 (65)	55 (69)	94 (62)	0.386
ECOG ≥2	31 (13)	5 (11)	26 (32)	0.010
LDH ≥Median (280)	88 (38)	34 (52)	54 (50)	0.756
Number of Metastatic Sites >2	110 (48)	42 (52)	68 (45)	0.333
Baseline Brain Metastasis	65 (28)	17 (21)	48 (32)	0.094
Received Palliative RT	139 (60)	46 (58)	93 (62)	0.574
Received Palliative Surgery	15 (6)	6 (8)	9 (6)	0.780

Table 2. Characteristics of 2L Therapy

	1L-ICI	1L-TT	P-Value
Received 2L Therapy	35 (44)	57 (38)	0.399
Reason for 1L Therapy Discontinuation			
Progression	30 (38)	85 (57)	<0.001
Toxicity	17 (21)	16 (11)	
Treatment Completion/Ongoing	18 (22)	11 (7)	
Unknown	15 (19)	38 (25)	
2L Therapy			
Anti-PD1	-	42 (74)	N/A
Anti-PD1 + Anti-CTLA4	-	15 (26)	
BRAFi + MEKi	35 (100)	-	
Reason for 2L Permanent Discontinuation			
Progression	22 (62)	30 (53)	0.619
Toxicity	3 (9)	4 (7)	
Treatment Completion/Ongoing	7 (20)	19 (33)	
Unknown	3 (9)	4 (7)	

Table 3. Multivariable Cox Analysis for Overall Survival

	Overall Survival		
	HR	95% CI	P-Value
Number of Metastatic Sites >2	2.230	1.432-3.474	<0.001
Baseline Brain Metastasis	1.317	0.841-2.062	0.228
Baseline ECOG≥2	2.666	1.667-4.263	<0.001
Sequencing Group (1L-TT as Reference)	0.669	0.415-1.078	0.098

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Thank You!

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