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## CLINICAL TRIALS IN GLIOBLASTOMA

### PRESENTATION OF THE PHILIPPINE LAUNCHING EVENT OF ONCOTHERMIA 2024.06.01.

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## CITATION

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Presentation of the Philippine Launching Event of Oncothermia 2024.06.01.  
<https://youtu.be/asHdJtezmic>.  
<https://www.youtube.com/playlist?list=PLEaAiXVgvMsEazu16PMNSqcJjZKF1yB3Y>

Oncothermia Journal 35, July 2024: 45–54.  
[https://oncotherm.com/MulhollandP\\_2024\\_Clinical-trials-in-Glioblastoma\\_20240601](https://oncotherm.com/MulhollandP_2024_Clinical-trials-in-Glioblastoma_20240601)



## Clinical Trials in Glioblastoma

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Consultant in medical oncology

UCL and UCLH



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- 1 UCLH
- 2 UCH Macmillan Cancer Centre
- 3 University College London, Cancer Institute

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# Research Overview



- Perspective on glioblastoma
- Past clinical trials
- Clinical trials in development
- Research group field of activity



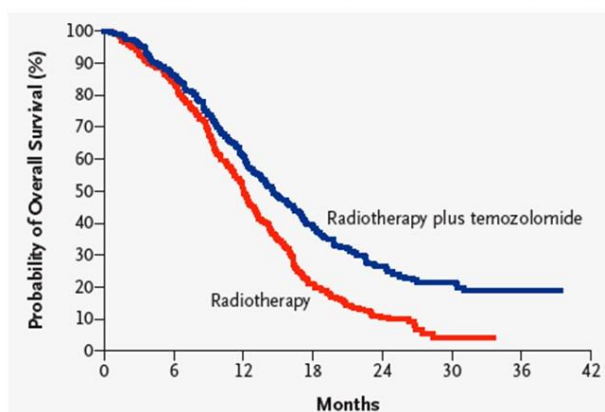
MRI  
diagnosis

Surgery

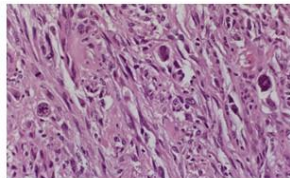
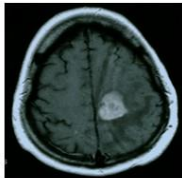
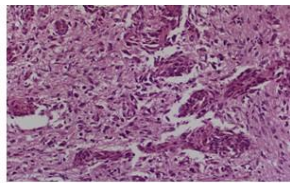
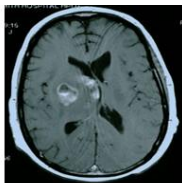
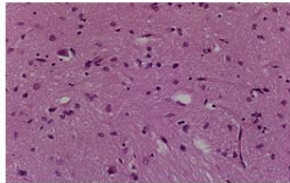
Chemo-  
radiation

Adjuvant  
treatment

Recurrent  
disease



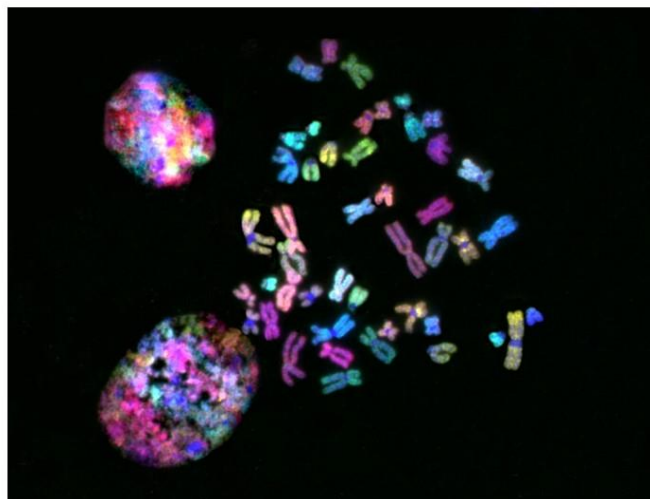
Glioblastoma  
Treatment  
Pathway and  
Clinical Trials



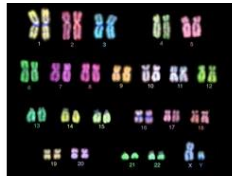
Tumour  
heterogeneity

## Chromosomal Architecture

Tania Jones  
Prof Sheer's Laboratory



Normal Male



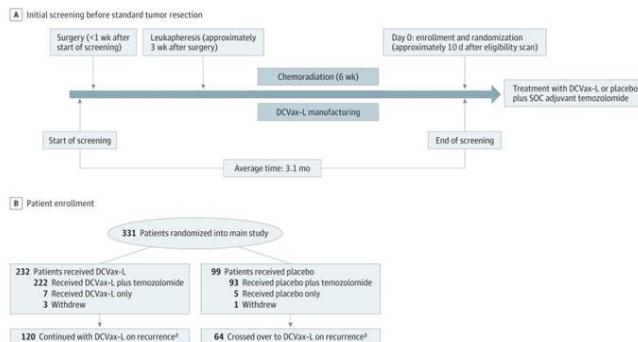
Glioblastoma



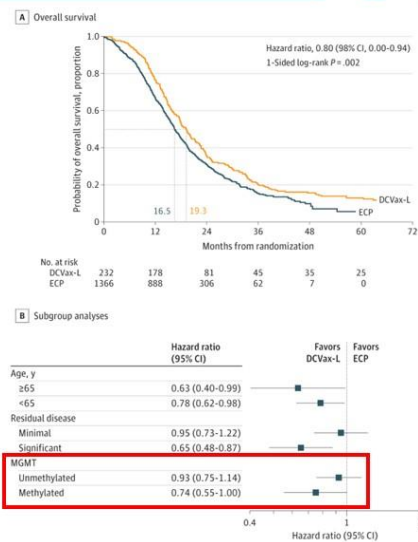
Mulholland et al. Cell Cycle 2005

- Resistant to most conventional treatment options, including chemotherapy, radiotherapy and molecularly targeted therapy.
- 'Promising' phase II results failing to be translated into encouraging phase III.
- Poor trial design, for example using historical data and not appropriate controls.
- The biology of glioblastoma is still not well understood.
- Improving our understanding of the molecular mechanisms driving this aggressive disease will allow development of more effective treatment.

## Immunotherapy: DCVax-L

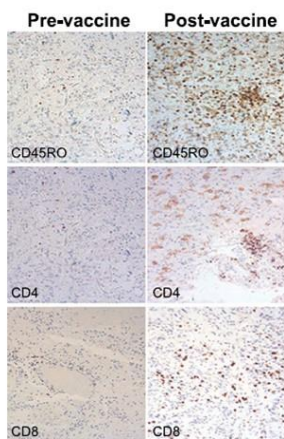


- DC vaccine added to SOC after chemoradiation
- Compared to matched historical controls
- Signal of activity in the MGMT methylated subgroup
- Licencing application submitted in the UK



Liau et al. JAMA Oncol, 2022





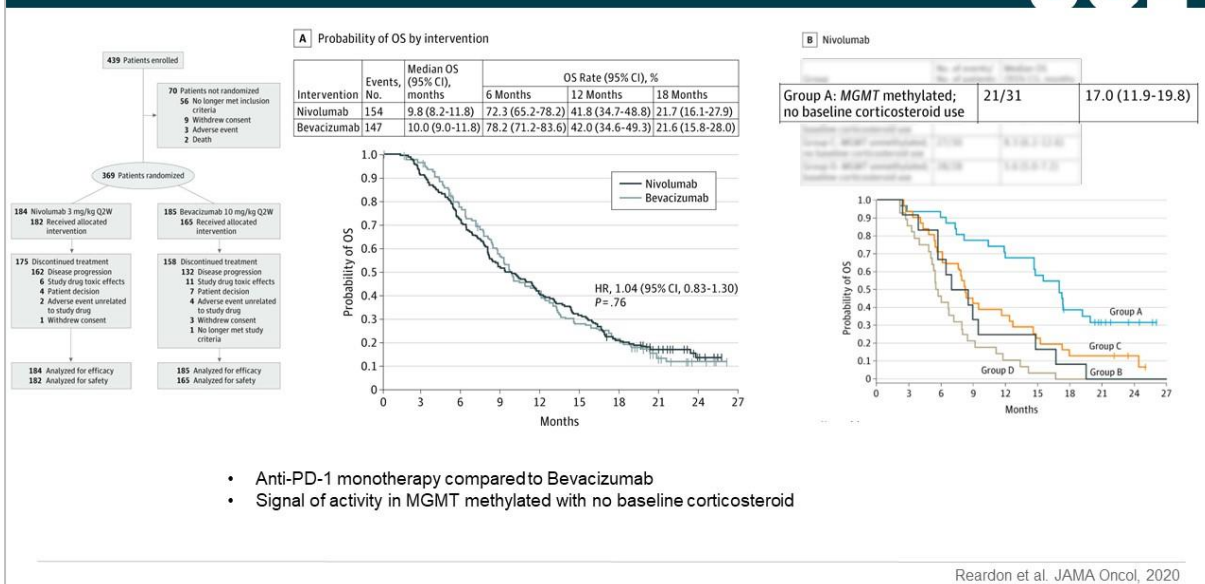
Infiltration of T cells into Glioblastoma tumors is observed in patients treated with DCVax®-L

Both CD4 and CD8 T cells are seen

## T Cells Can Cross the Blood Brain Barrier; T Cells Infiltrate Glioblastoma Tumors After DCVax-L

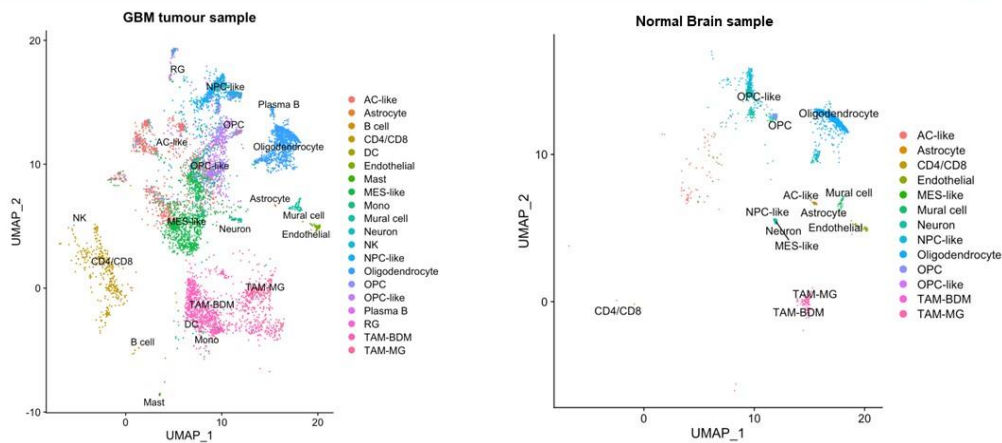
L. Liau et al.

## Immunotherapy CheckMate 143



- Anti-PD-1 monotherapy compared to Bevacizumab
- Signal of activity in MGMT methylated with no baseline corticosteroid

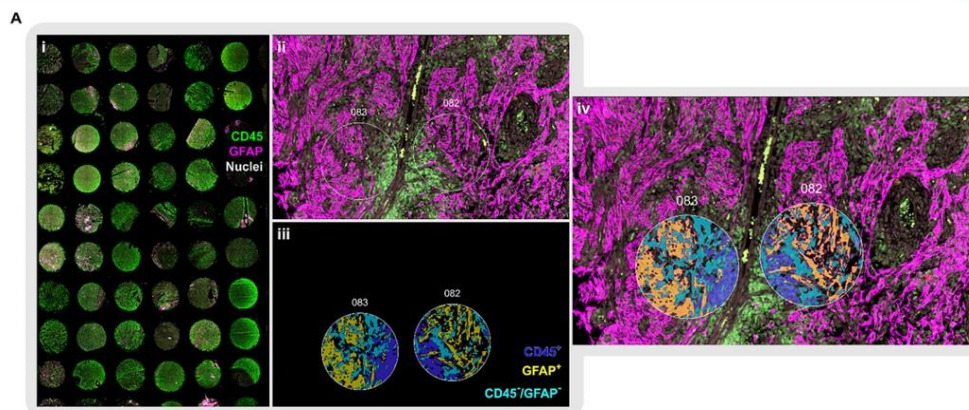
## Lab – Correlative studies



- Single-cell analysis allows to characterize the tumour cells and surrounding cells complexity
- UMAP artificially plots the composition of identified cell subtype

Unpublished, Wang et al., Cancer Cell, 2021; Ruiz-Moreno et al., bioRxiv, 2022

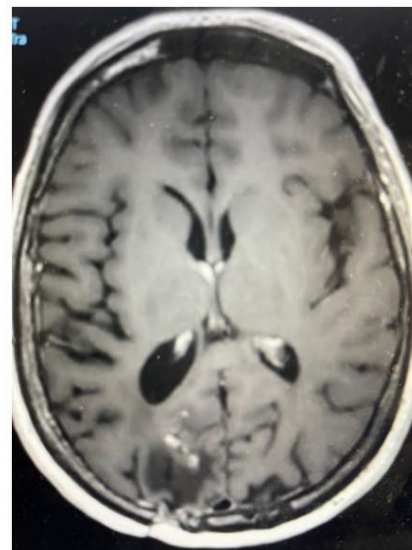
## Lab – Correlative studies



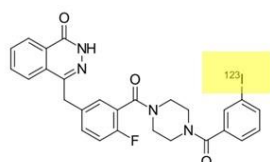
- Spatial-transcriptomics allows the same analysis genomic analysis while preserving the tissue architecture
- Enables to identify location-specific cell subtype interactions

Bonnett et al., Cancer Res Commun, 2023

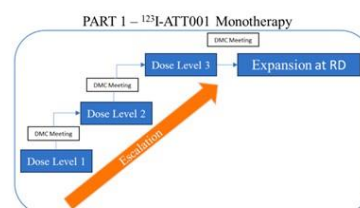
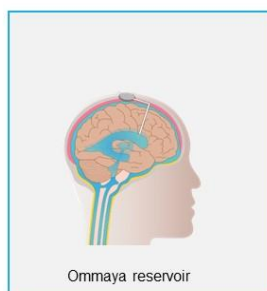
Started using the device in January 2023  
Treated 27 patients so far







**Figure 1** Chemical structure of  $^{123}\text{I}$ -ATT001



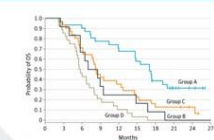
**Figure 1** CITADEL-123 study design (Part 1)

**A Phase I clinical trial to assess the activity of I-123 Poly Adenosine Diphosphate Ribose Polymerase I inhibitor (123I-ATT001) directly administered in subjects with relapsed glioblastoma.**

1. Feasibility Phase II study of Standard of Electro-hyperthermia plus Standard of Care
2. Feasibility Phase II study Checkpoint inhibitor prior to Standard of Care in Glioblastoma
3. Following the feasibility studies: Phase II study of Checkpoint inhibitor plus Electro-hyperthermia
4. Citadel -123 Plus Electro-hyperthermia

Clinic

- Clinical trials for patients with GBM
- Access to post-treatment samples



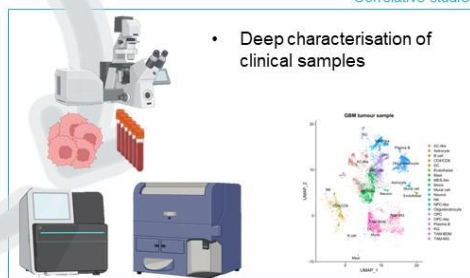
Experimental work

- Hypotheses driven by clinical work
- Developing new strategies to test in the clinic



Correlative studies

- Deep characterisation of clinical samples



Thank you for your time

Glioblastoma is very challenging to treat  
Targeted therapies not been effective  
There has been benefit seen with immunotherapy

We need to systematically test agents in clinical trials and we need to explore the full potential of electro-hyperthermia