QBiotics Group

Tigilanol Tiglate

Oncolytic small molecule for intratumoural treatment of solid tumours

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QBiotics Group

QBiotics Group company overview

QBiotics Group

Australian unlisted life sciences company

Specialists in plant-derived, cell signalling small molecules

Founded Discovery Co. 2000; Development Co. 2010

EcoLogic™ unique discovery platform

Focus on two high value, first-in-class programmes in **oncology & wound healing**

Sound scientific expertise

Team of 59 employees

6 PhD, 1 MD, 1 DVM (oncology) 5 BVSc, 9 BSc

Global contracts

Clinical and Scientific Advisory Boards

7 Universities

2 Research Institutes

49 CRO/CMO providers and advisors

Focus oncology and wound healing

Oncology - solid tumours clinical Phase II

- Soft tissue sarcoma
- Head and neck cancer

Wound healing – chronic/acute, burns clinical Phase I

- Venous leg ulcers

Discovery programs in antibiotics and anti-inflammatories

Veterinary data underpins human programs

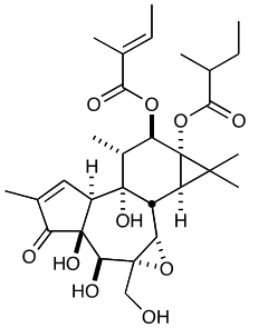
Informs and derisks early-stage human clinical

- STELFONTA registered for canine MCT
- Approved FDA-CVM, EMA, VMD, APVMA
- Marketed by Virbac

Sound IP coverage with composition of matter and use patents on all products

Tigilanol tiglate novel expoxytigliane overview

Seeking a partner for development of the human programme



Unique and differentiated MoA

- Pan tumour
- Single IT injection
- Rapid tumour destruction
- Site healing
- Systemic anti-tumour immune response

Clinical Phase I trials sound data

- Well tolerated
- MTD not reached
- Activity in nine tumour types
- ICD markers and CD8+ T cell infiltration in human HNSCC tumour biopsies

Two Phase II trials current

- Soft tissue sarcoma
  - MSKCC USA
  - Patient recruitment finalised
  - FDA Orphan Drug Designation
- Head and neck cancers
  - Royal Marsden
  - 5 sites UK, 2 sites AU

Regulatory and Commercial validation in veterinary market

STELFONTA®

- Canine MCT
- USA, UK, EU & AU

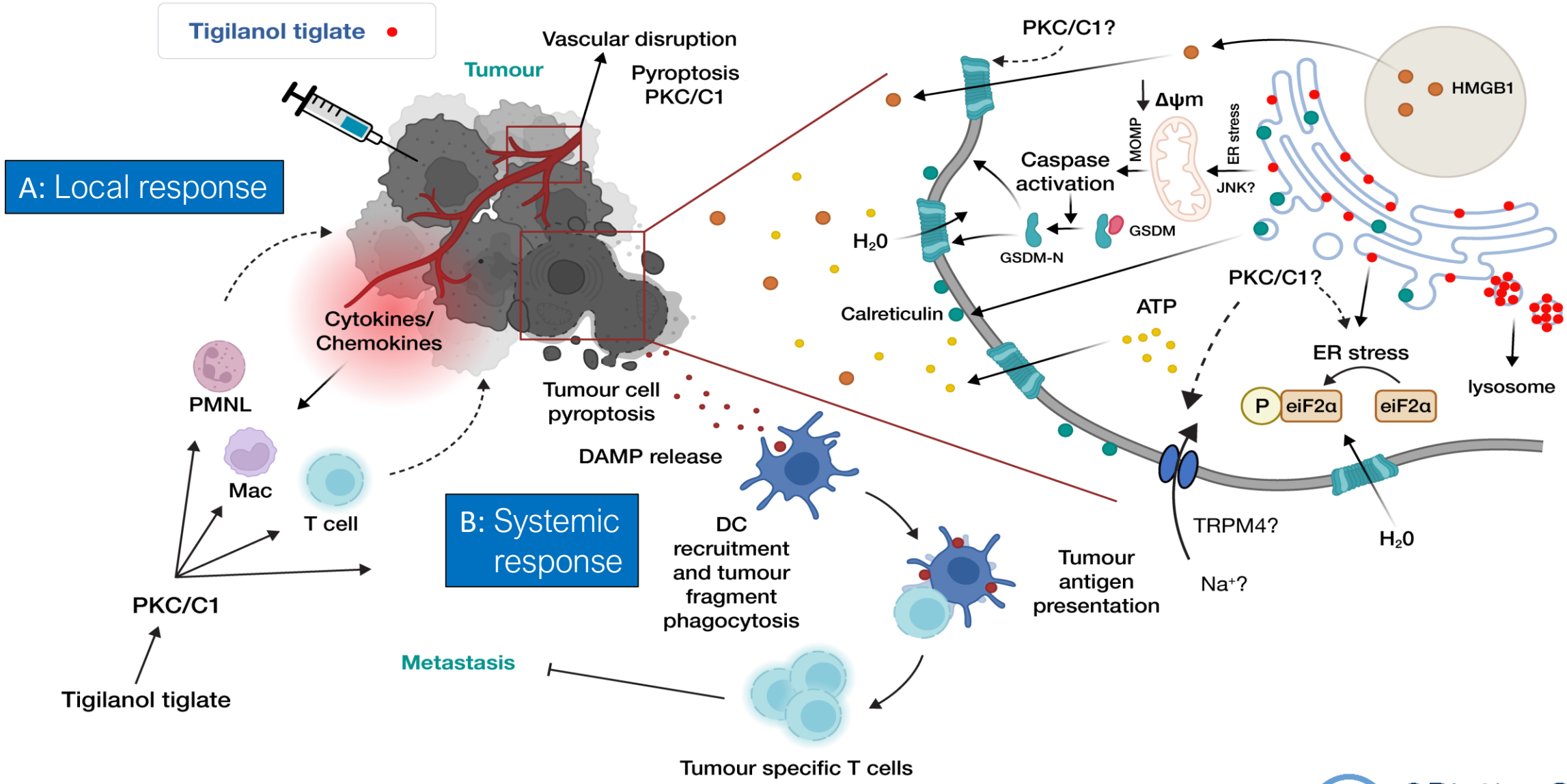
Commercial Qualities

- Commercial manufacturing & supply
- Comparative low COG
- Simple to use
- Good stability drug product
  - ✓ 4+ years 2-8 °C
  - ✓ 12 months RT
- Sound patenting profile

Significant Growth Opportunities

- Multiple tumour indications
  - External and internally located
- Late and early settings
- Strong monotherapy activity
- Combination potential ICI, chemotherapy, radiotherapy

Tigilanol tiglate mode/mechanism of action



Boyle *et al.* 2014. PLoS ONE 9(10); Cullen *et al.* 2021. *Scientific Reports.* https://doi.org/10.1038/s41598-020-80397-9
Cullen *et al* 2024. *Journal for Immunotherapy of Cancer*, *12*(4).

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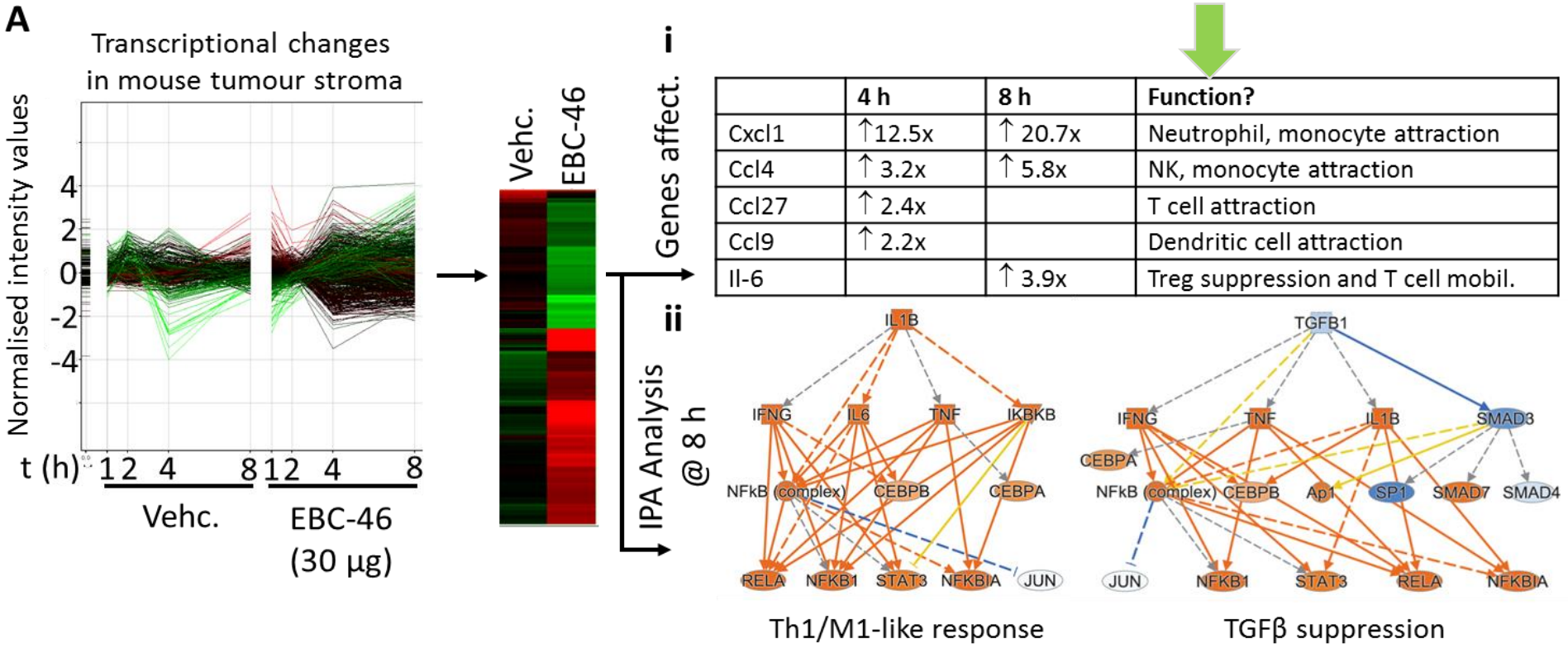
MOA: Induces rapid upregulation of genes associated with immunological responses

Induction of pro-immunogenic Th1/M1-like response



	4 h	8 h	Function?
Cxcl1	↑12.5x	↑ 20.7x	Neutrophil, monocyte attraction
Ccl4	↑ 3.2x	↑ 5.8x	NK, monocyte attraction
Ccl27	↑ 2.4x		T cell attraction
Ccl9	↑ 2.2x		Dendritic cell attraction
Il-6		↑ 3.9x	Treg suppression and T cell mobil.

Th1/M1-like response

TGFβ suppression

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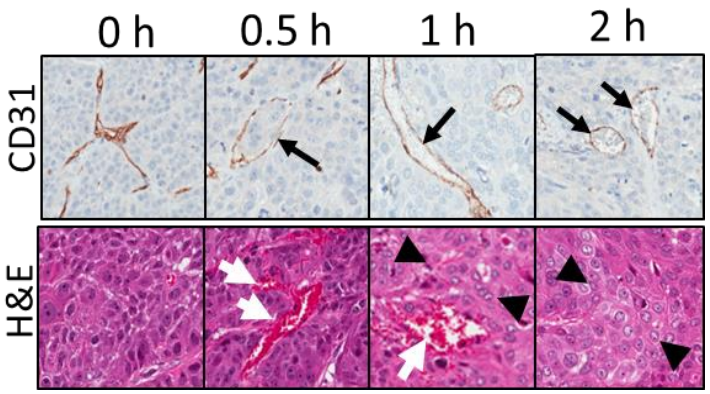
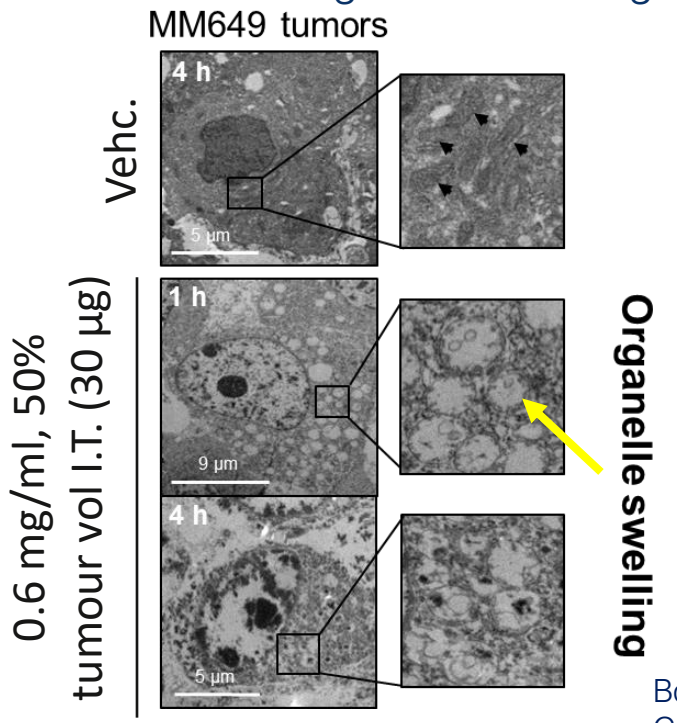
MOA: Induces oncosis/pyroptosis in endothelial and cancer cells

Induces vascular disruption



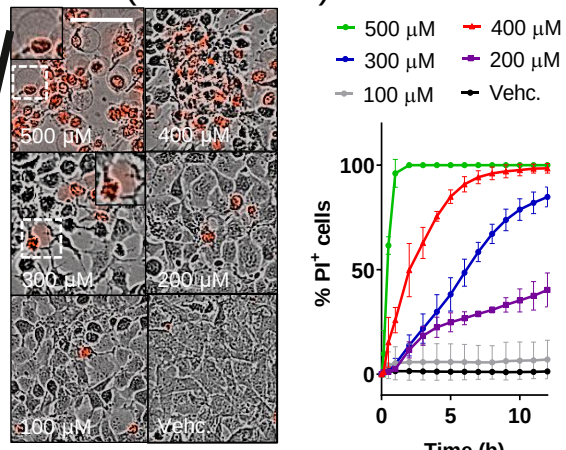
Induces organelle swelling



Promotes death of tumour and endothelial cells

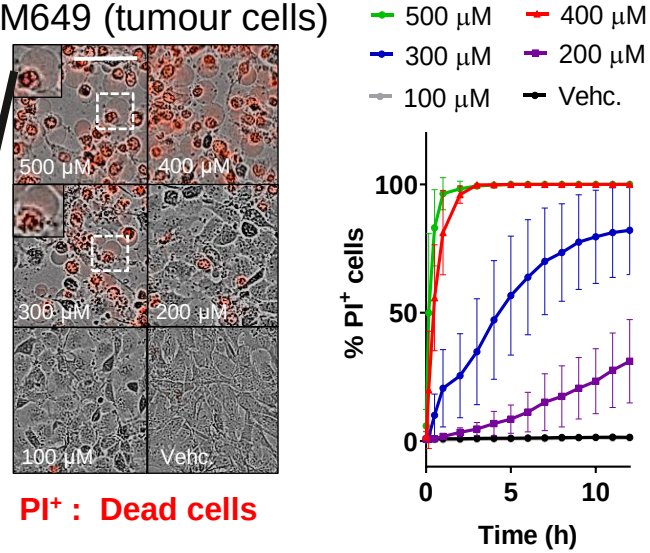
In vitro

2H-11 (endothelial)



PI⁺ : Dead cells

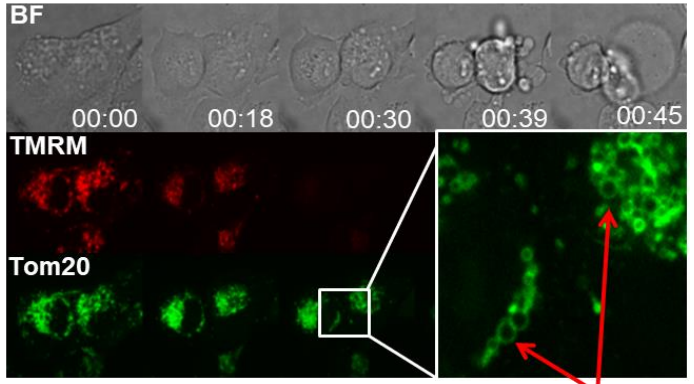
MM649 (tumour cells)



PI⁺ : Dead cells

Induces cellular oncosis

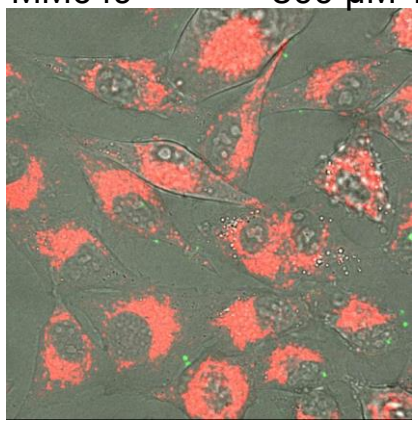
500 µM TT



Mitochondrial swelling

In vivo

MM649 500 µM TT



TT = tigilanol tiglate

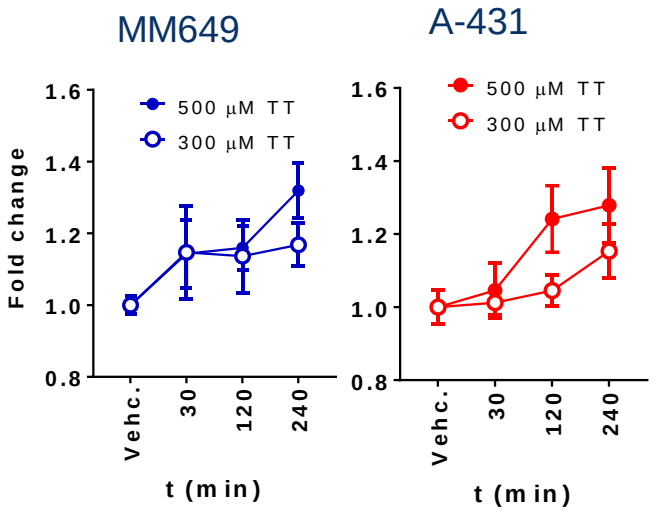
mito ΔΨm

Memb. rupture

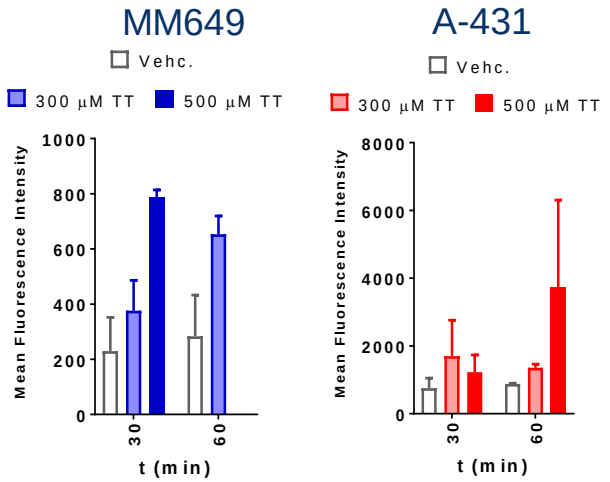
Boyle *et al.* 2014. PLoS ONE 9(10); Cullen *et al.* 2021. *Scientific Reports.* https://doi.org/10.1038/s41598-020-80397-9
Cullen *et al* 2024. *Journal for Immunotherapy of Cancer*, *12*(4).

MOA: Induces immunogenic cell death

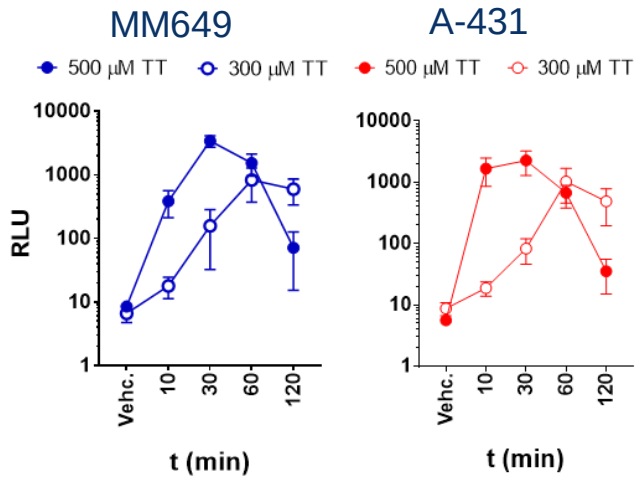
HMGB1 release



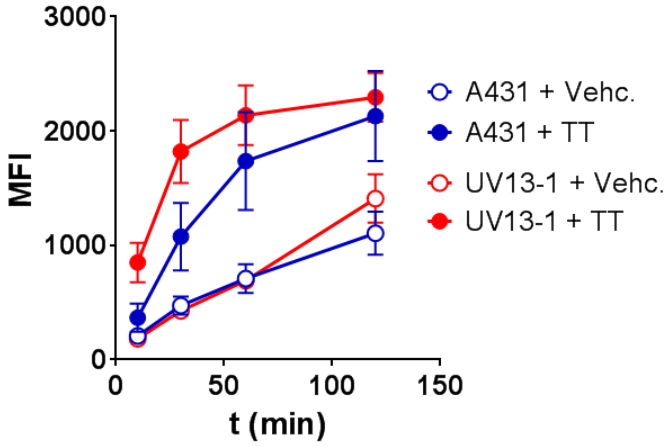
Calreticulin externalisation



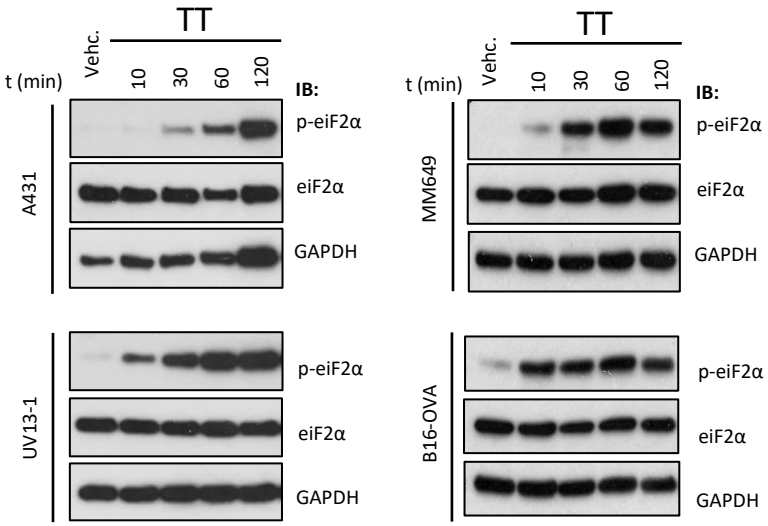
ATP release



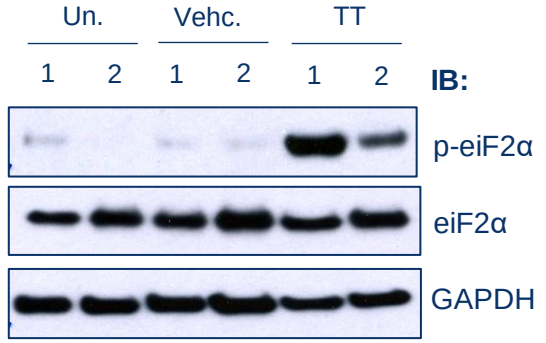
ROS production



Unresolved ER stress



eiF2alpha phosphorylation *in vivo* in MM649 tumour xenografts

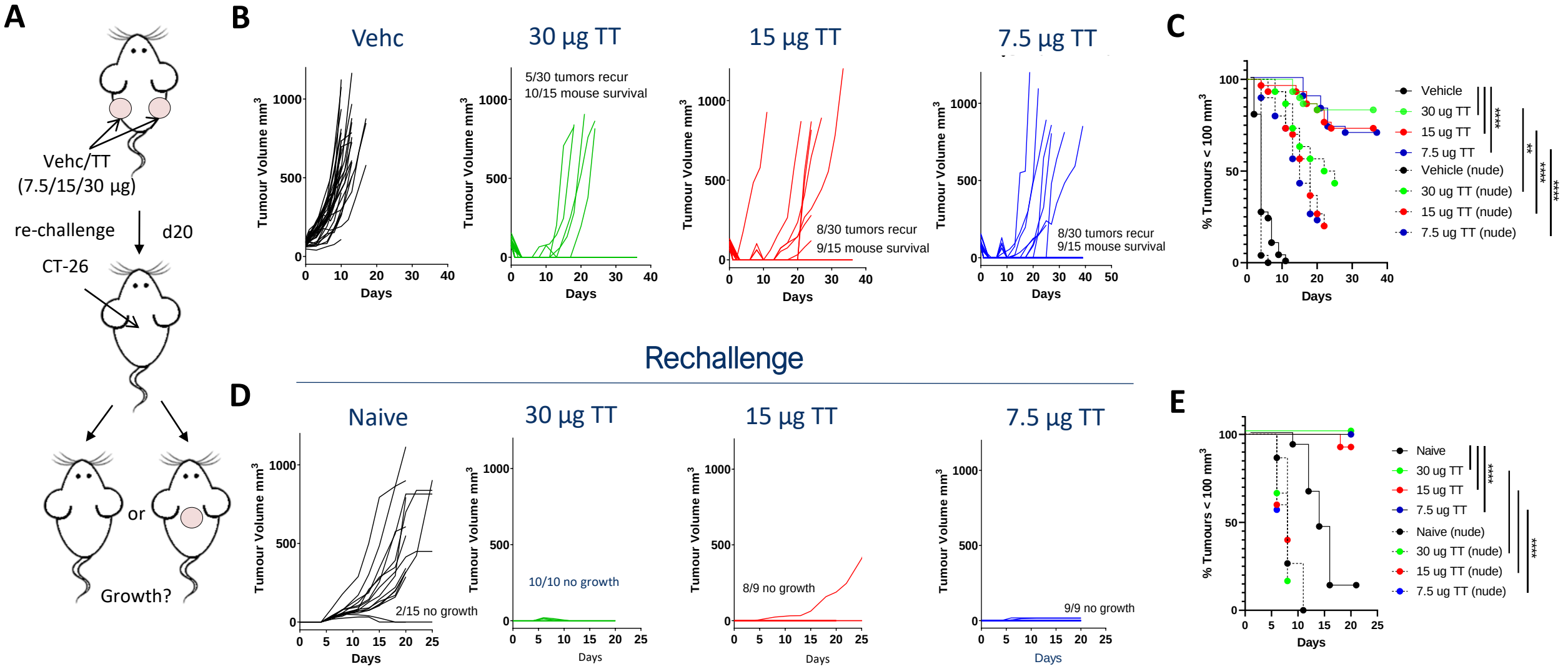


TT = tigilanol tiglate

Cullen *et al.* 2021. *Scientific Reports.* https://doi.org/10.1038/s41598-020-80397-9; Cullen *et al* 2024. *Journal for Immunotherapy of Cancer*, *12*(4).

MOA: Induces immunological memory

Protects against distal tumour growth



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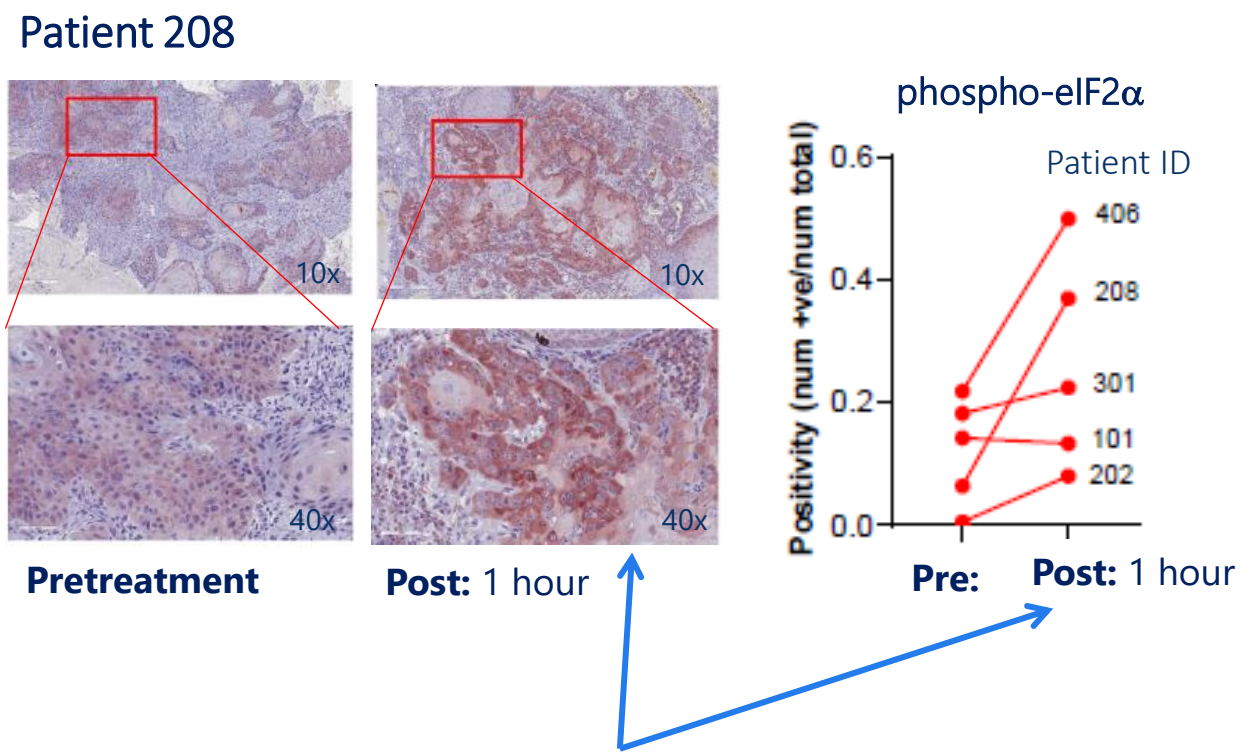
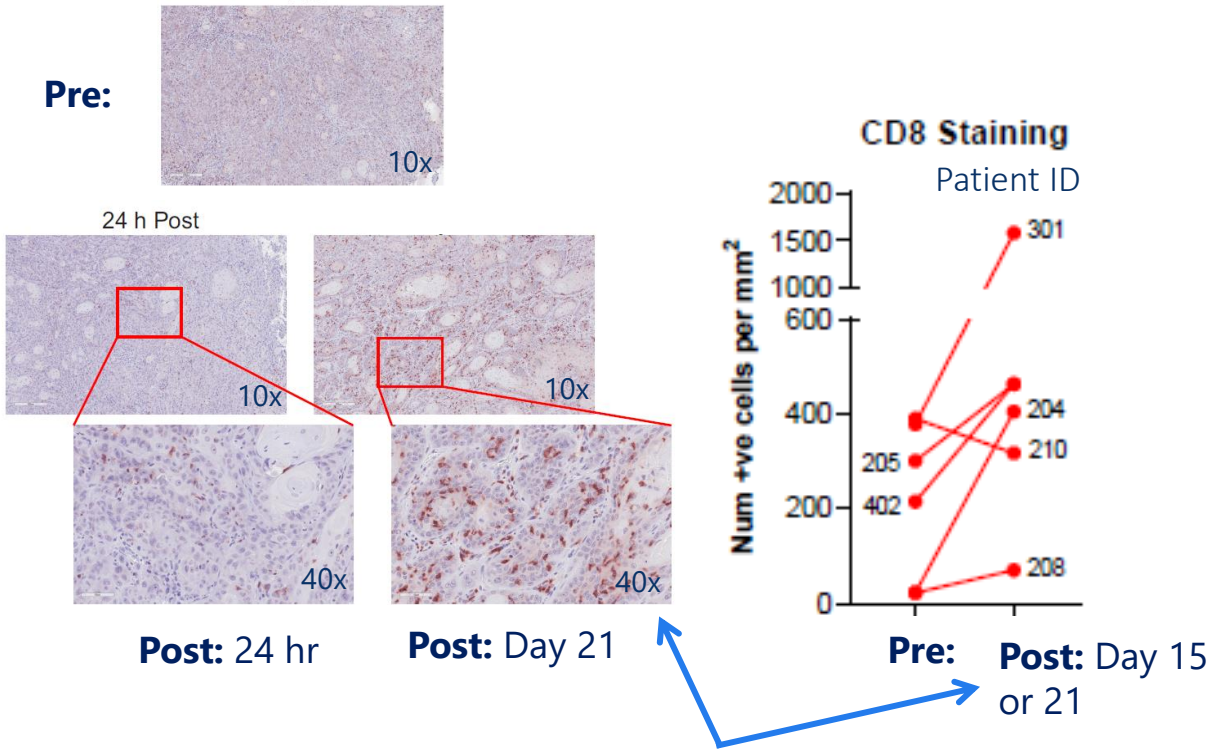
ICD indication and T cell infiltration in treated human patient biopsies

QB46C-H03 (ACTRN126190014071 89) Phase I/IIa HNSCC window of opportunity before surgery; 19 patients





Increased phosphorylation of eIF2α (pathognomonic marker of ICD) in HNSCC biopsies 1 hour post treatment

Increased CD8⁺ T cell infiltration in HNSCC tumours surgically excised at Day 15 or 21

TT = tigilanol tiglate

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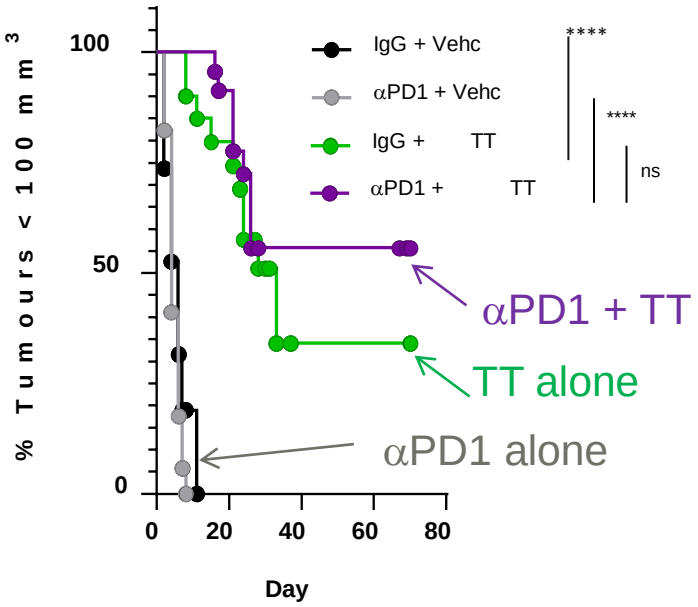
Significantly improves survival in murine studies when combined with ICI, chemotherapy and radiotherapy

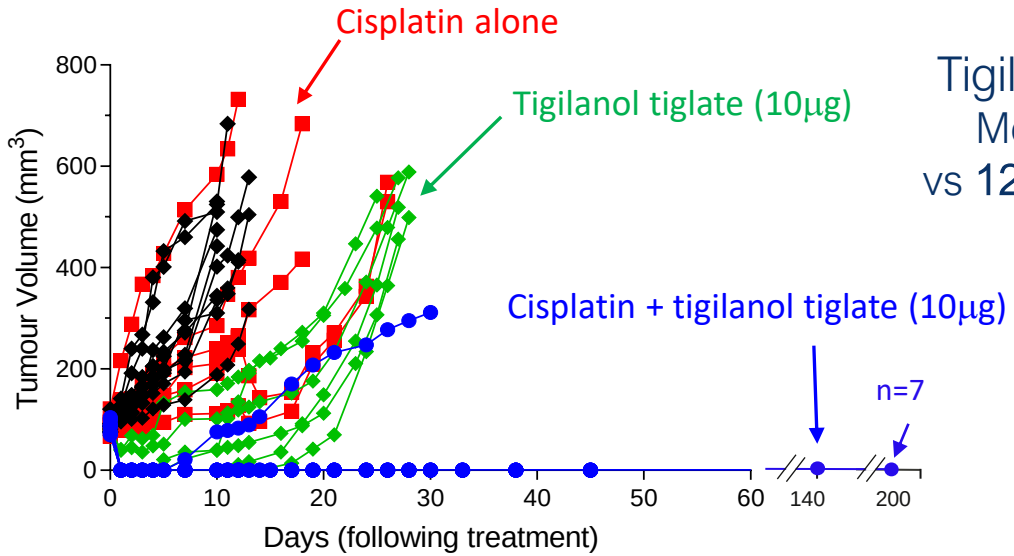
Tigilanol tiglate + αPD-1
increases survival and regresses tumours in ICI refractory melanoma



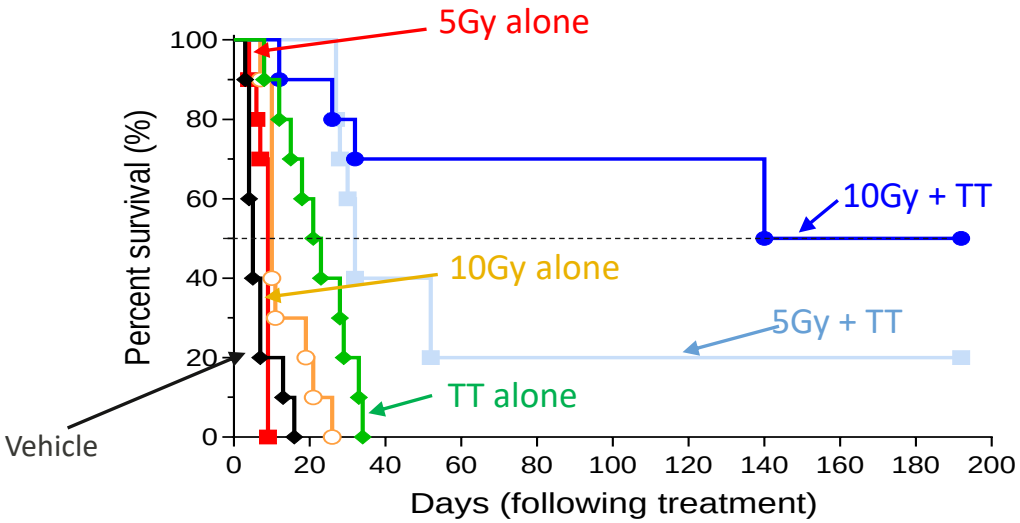
N=10 animals per group. ****p<0.0001; Log rank (Mantel-Cox) test

*****p<0.000001; ****p<0.00001; **p<0.001.

TT = tigilanol tiglate



Tigilanol tiglate + Cisplatin
Median survival **193 days**
vs **12 days** with Cisplatin alone



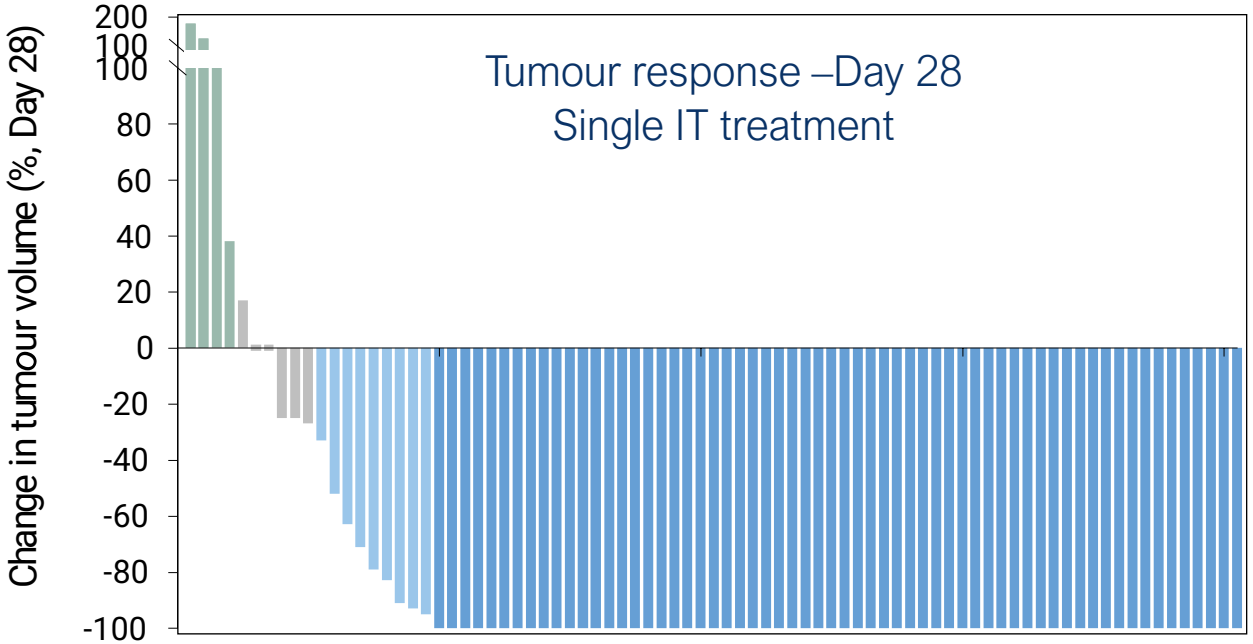
Tigilanol tiglate + radiotherapy
Median survival **166 days** vs **10 days** with radiotherapy alone

Cullen *et al.* 2021. *Scientific Reports.* https://doi.org/10.1038/s41598-020-80397-9; Cullen *et al* 2024. *Journal for Immunotherapy of Cancer*, *12*(4).

Impressive results in dogs

Canine US FDA-CVM registration trial

Single treatment induces Complete Response in 75% canine mast cell tumours
Fully blinded and controlled 123 patient trial



Tumour response in tigilanol tiglate treated dogs (n=81)

- 75% CR single IT treatment (p<0.0001 vs sham control)[1]
- Objective Tumour Response Rate (CR/PR) of 80%
- 88% CR with second treatment for partial responders
- No tumour recurrence 89% of evaluable cases (n=57) at 12 mths

Progression of clinical response in canine case US FDA-CVM registration trial - subcutaneous MCT

Pretreatment

Day 1: Tumour haemorrhagic necrosis

Day 7: Complete Response

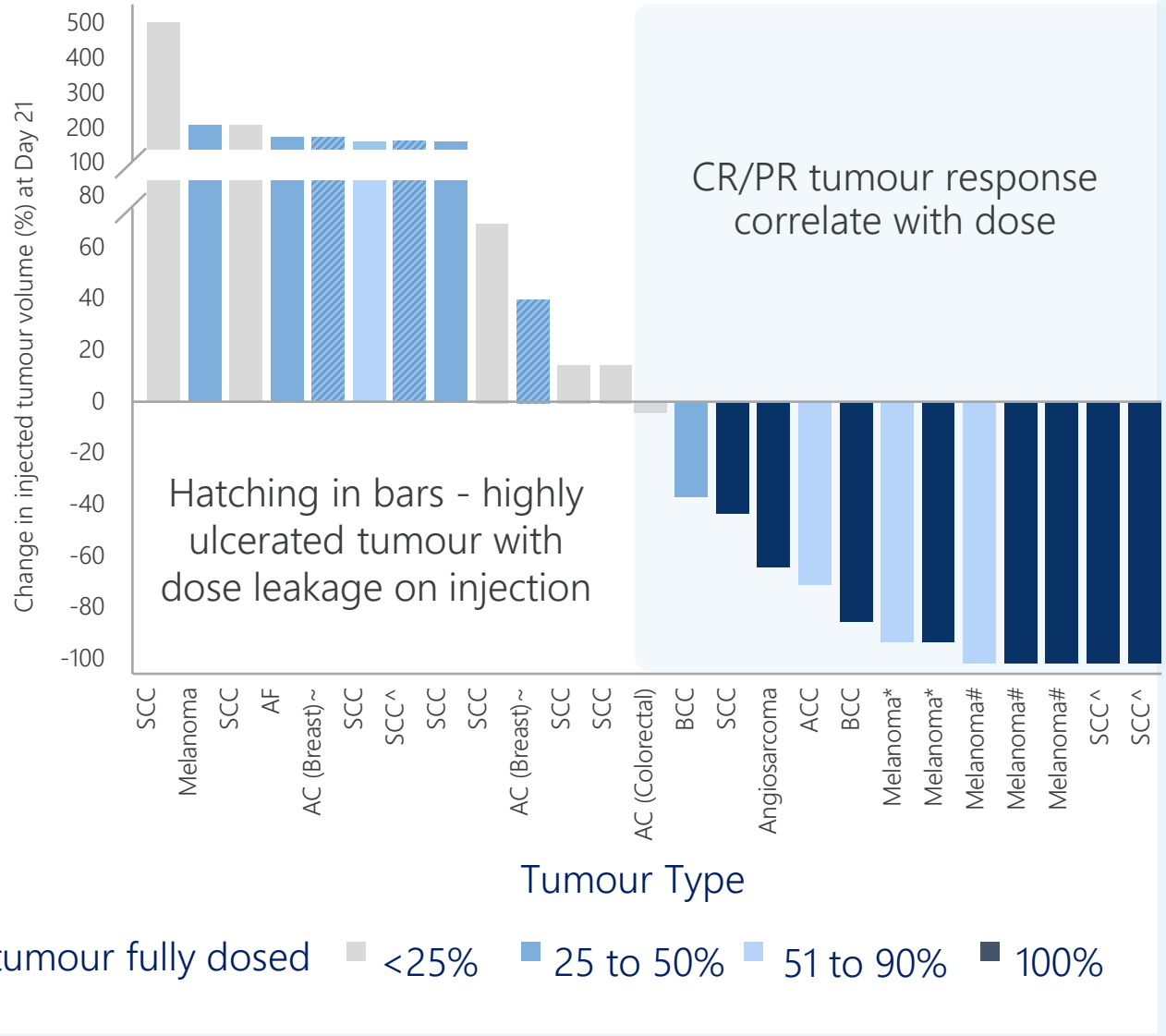
Day 28: Site healed

[1] De Ridder *et al* 2021. *Journal of Veterinary Internal Medicine*, *35*(1):415-429.

Safety and efficacy demonstrated in Human Clinical Phase I trial

QB46C-H01/2: open label, multicentre, single arm dose escalation (3+3)
Single tigilanol tiglate IT injection

- Advanced refractory skin & subcutaneous tumours
- 22 patients – Day 28 assessment
- IT based on mg drug/kg BW, not tumour volume as per cases of intent to treat (%v/v)
- Most AEs expected/desired re MOA
- MTD not reached - final dose 3.6 mg/m^2
- **Signs of efficacy in all 9 tumour types treated**
- CR at optimal dose
- Abscopal response distal tumours 2 patients



Panizza B. *et al.* EBioMedicine, 50 (2019). 433 - 441

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Example cases QB46C-H01/2

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Patient 407 - Angiosarcoma – failed multiple surgeries - *recommendation of total rhinectomy*

Single IT treatment
- CR & organ preservation
- Patient disease free (CT scan) at 25 months
- Clinically disease free at 30 months

Pretreatment

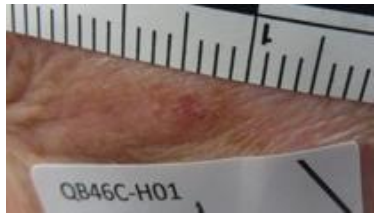
Day 2: Tumour necrosis

Day 15: Necrotic tumour slough

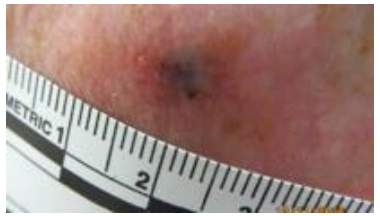
Day 43: Complete response[2]

Patient 202 - Squamous Cell Carcinoma - failed radiotherapy, cetuximab, cisplatin, 5FU > 7 mths prior to treatment

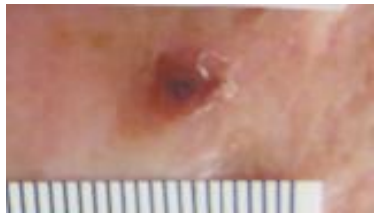
Single IT treatment
- Complete Response at Day 15
- No scarring



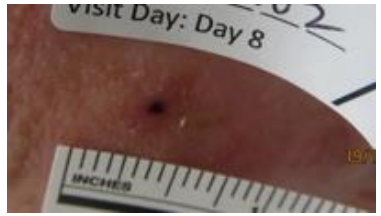
Pretreatment



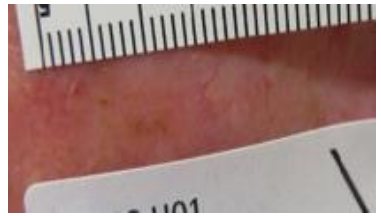
Day 1: Tumour necrosis



Day 5: Tumour destruction almost complete



Day 8: Tumour destruction almost complete



Day 15: CR, good cosmesis

[1] Panizza B. *et al*. *EBioMedicine*, 50(2019). 433 - 441
[2] Reported off study by Panizza et al., 2019.

Example cases QB46C-H01/2

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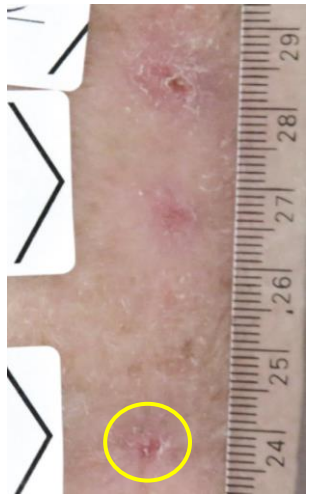
Patient 102: Metastatic melanoma

Pretreatment

Day 1: 30 mins: tumour necrosis

Day 8: Non-injected, 4th tumour regresses



Day 35: CR injected a non-injected tumour

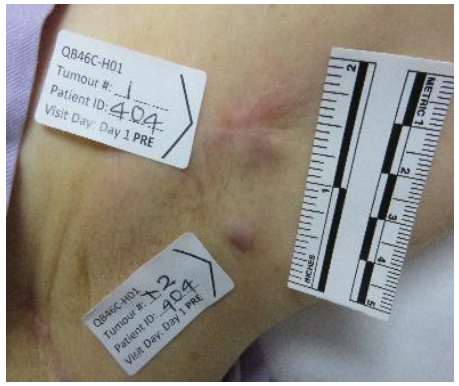
Single IT injection

- Into top 3 tumours - 4th tumour (circled) not treated

Abscopal response in:

- Lung & sternum tumours regression reported off study as an abscopal effect

Patient 404: Metastatic melanoma - failed ICI and multiple surgeries



Pretreatment

Day 2: Tumour necrosis

Day 29: Complete Response

24 months: Patient tumour free

Single IT injection into 2 tumours in axila

Abscopal response in:

- Contralateral parotid nodal deposit and leg melanoma - both cleared
- Patient clinically and ultrasound clear at 33 months post-treatment

Panizza B. *et al*. *EBioMedicine*, 50(2019). 433 - 441

Tigilanol tiglate current development status - IT monotherapy

QB46C-H07 (NCT05755113) Phase II pilot STS

FDA Orphan Drug Designation

- Open-label trial US FDA IND
- Preliminary efficacy & safety – 10 patients advanced and/or metastatic STS
- Tumour ablation Day 28; local recurrence 6 months

Patient recruitment finalised

Presenting data at BARCELONA 2024 ESMO congress

Memorial Sloan Kettering Cancer Center USA

QB46C-H08 (NCT05608876) Phase II Head & Neck Cancer

- Open-label single arm trial UK MHRA CTA; AU CTN – 5 sites UK, 2 site AU;
- Simons 2 stage – recurrent &/or metastatic - 37 patients
- Tumour ablation Day 28
- PFS (RECIST v1.1) ORR (RECIST v1.1 and itRECIST) up to 18 months

12 patients recruited

Lead site: The Royal Marsden Hospital UK

Compassionate Use

- Gustave Roussy Cancer Centre Paris
- Kinghorn Cancer Centre Sydney

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Thank You

For further information:

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