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What is the problem?

~90%
of patients face recurrence within two years of the initial diagnosis

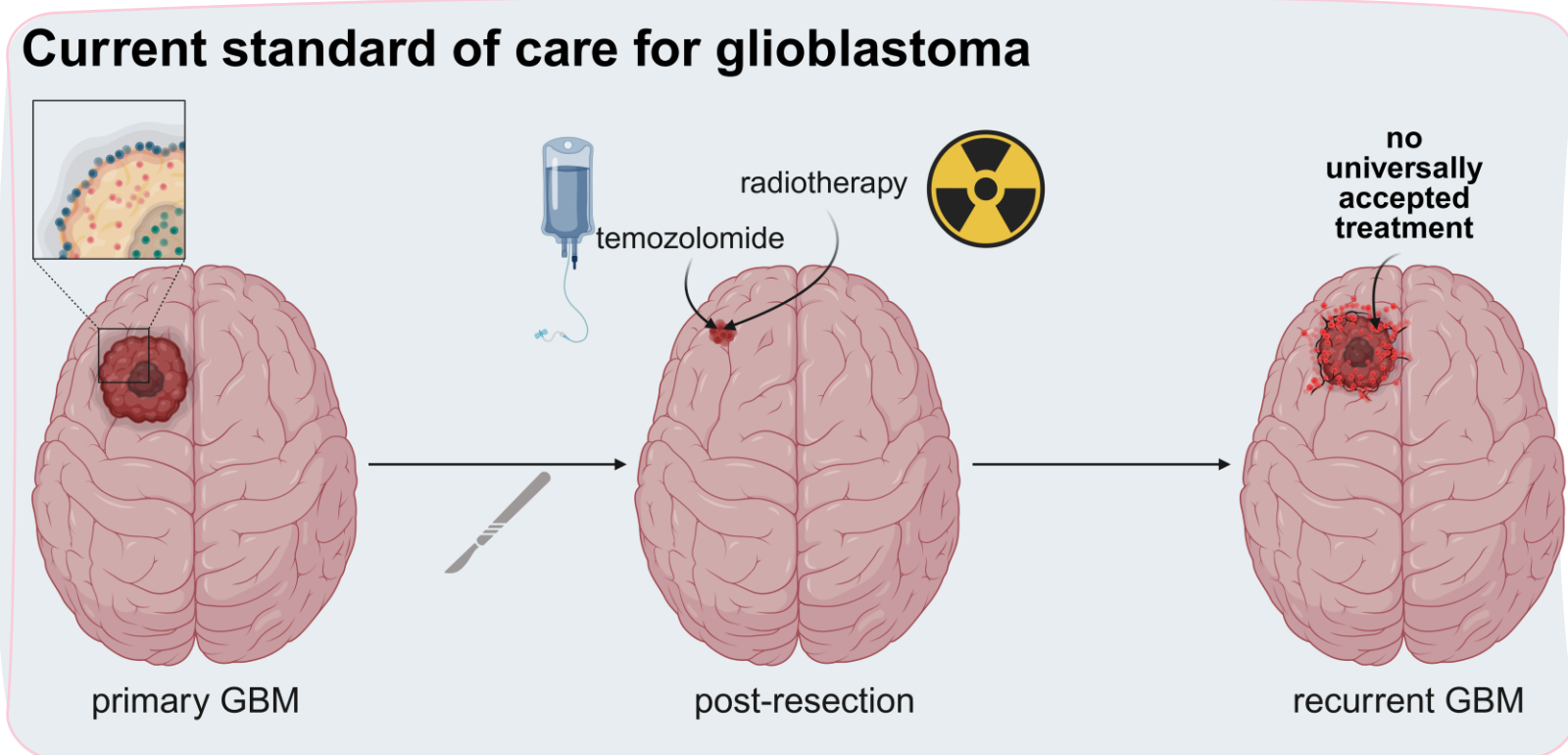
<13%
survival rate after 5 years. One of the worst prognoses

#1
cause of cancer-related death in patients under the age of 40...

...and yet, only **3.2%**
of national cancer research funding is allocated to them

“There needs to be a better roadmap for recurrence.”

“I feel like I’m a dead man walking.”



Our aim is to develop a novel combination strategy to prevent glioblastoma recurrence using a 3-pronged approach.

What is our strategy?

OUR 3-PRONGED APPROACH TO TARGET RECURRENCE

inhibit internal energy production
target an enzyme involved in cell metabolism, with new inhibitors.

target with high dose-rate radiotherapy
utilise FLASH-radiotherapy, therapeutic radiation delivered ultra-fast.

manipulate immune system to attack
encourage hijacked immune cells to be tumour-suppressive instead of -supportive.

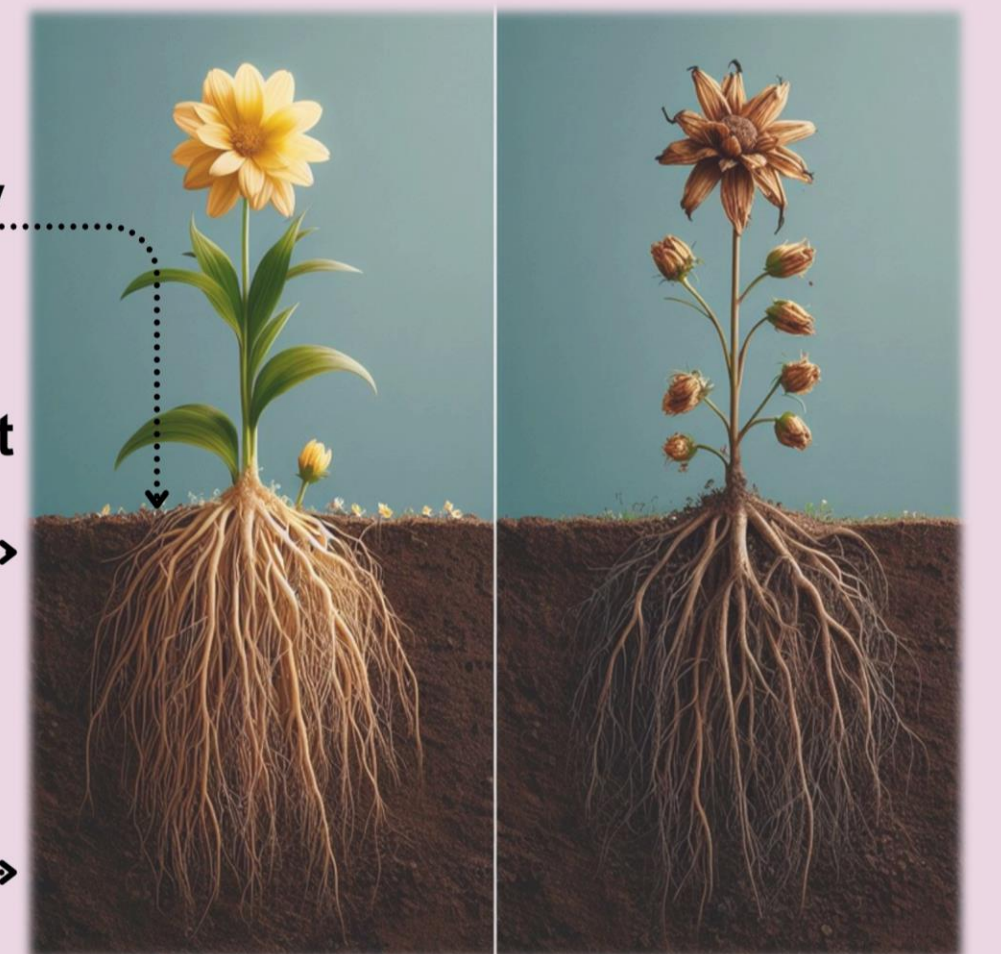
‘What does this mean?’

A glioblastoma behaves like a weed in rich soil

we can weaken the roots by blocking how these remaining cancer cells make energy

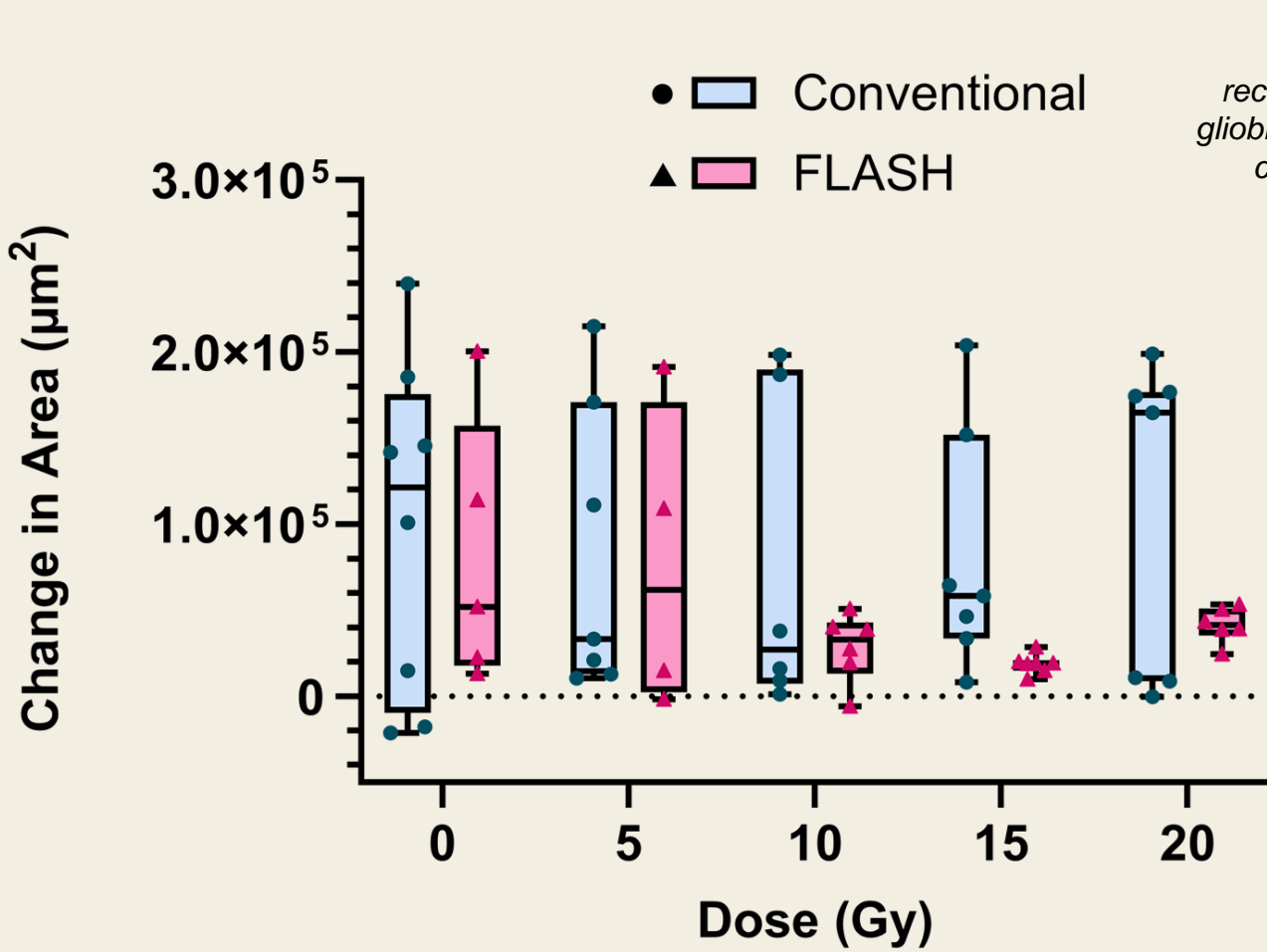
FLASH radiotherapy acts like pouring boiling water on the weed, shocking the root system and slowing regrowth

we can poison the soil by controlling the signals the tumour sends out



What did we find?

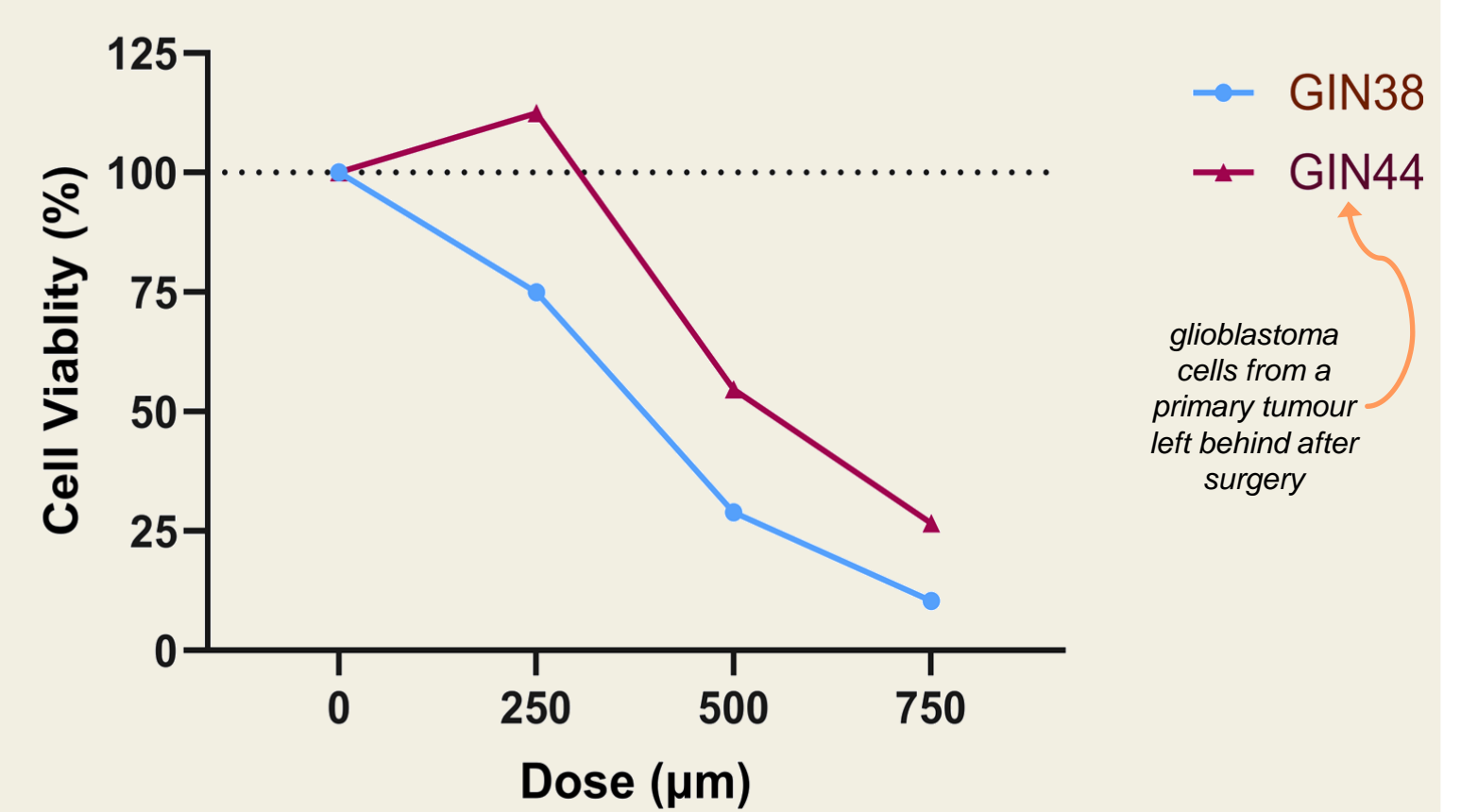
Effect of FLASH vs conventional radiotherapy on GIN98R



Metabolic inhibitor 3-bromopyruvate effectively **reduced tumour viability** in a spheroid model (mini tumour), made with glioblastoma cells (GIN38/GIN44).

FLASH radiotherapy seems to **control the area** of glioblastoma spheroids (mini tumours) **more effectively** than ‘conventional’ radiotherapy, at doses of 10Gy and above. This effect is observed in tumour cells that appear **radioresistant** (GIN98R).

Effect of 3-bromopyruvate on tumour cell viability



Take home message:

We have reduced the viability of glioblastoma cells left behind after surgery by targeting their energy production, and shown that they respond to ultra-high dose-rate radiotherapy. Next, we will combine these two approaches to explore the benefits of a potentially synergistic and most importantly, kinder, treatment.

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References

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