eha Sf(PM)

Overcoming venetoclax resistance in acute myeloid leukemia by selective PARP1 inhibition

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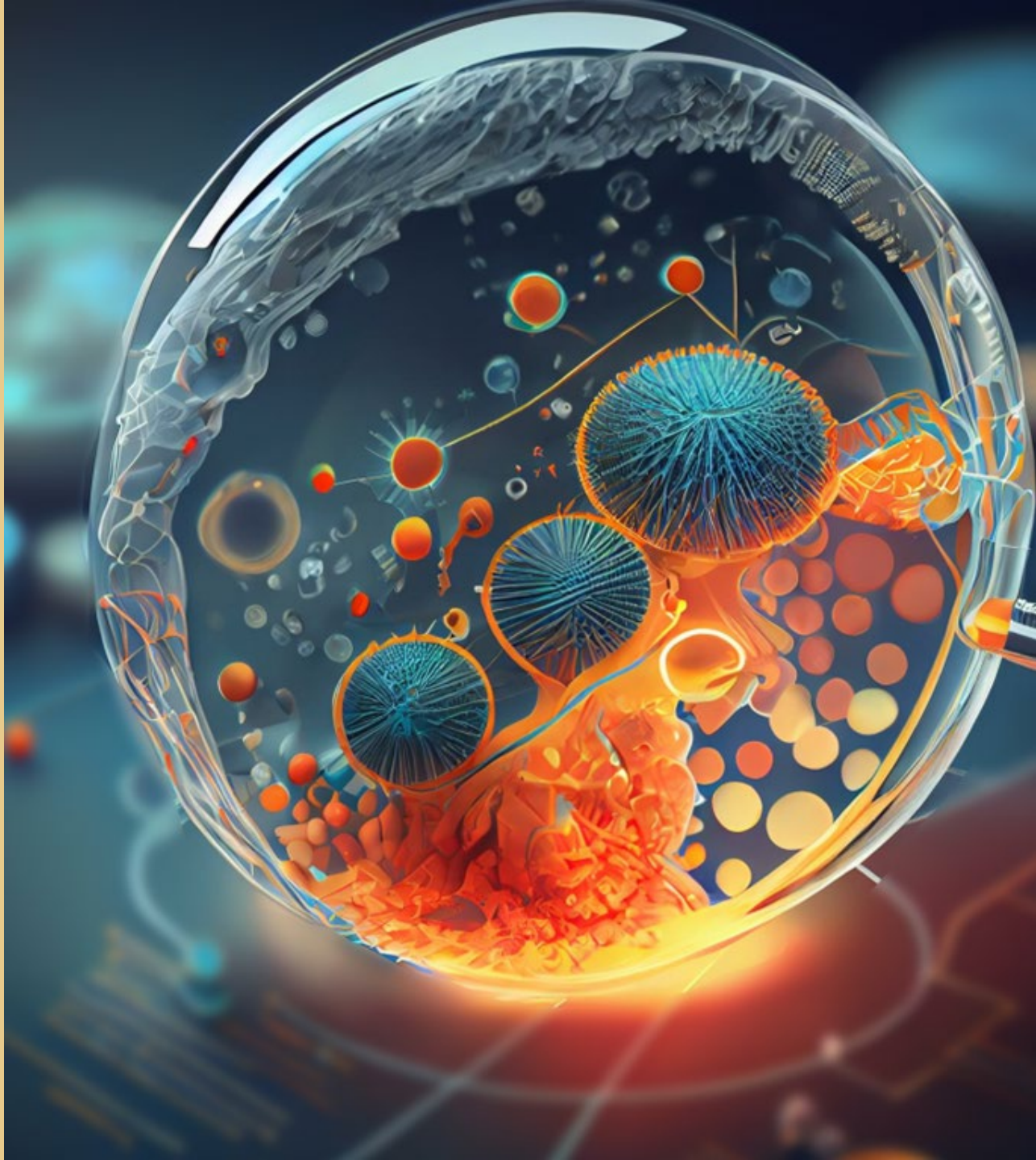
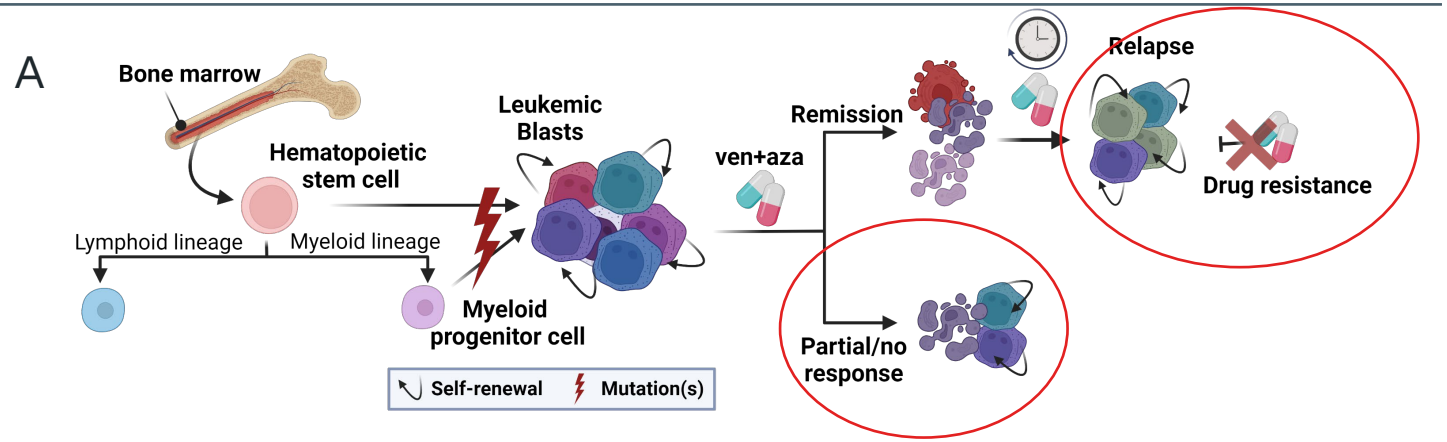
26th September 2024

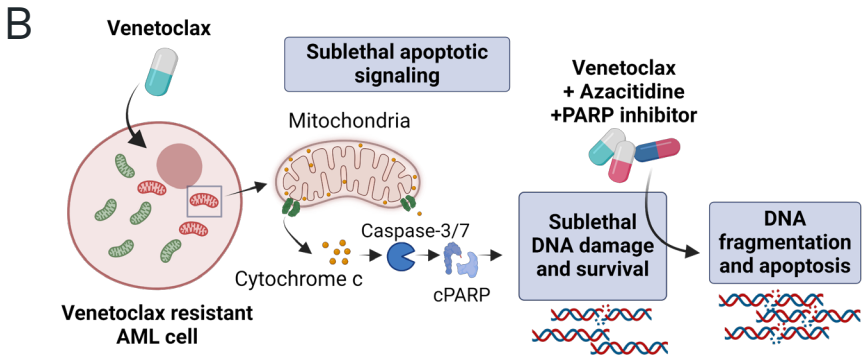


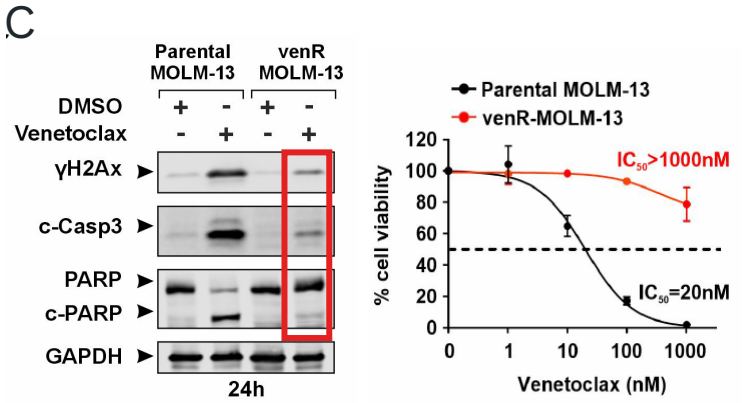
ACUTE MYELOID LEUKEMIA (AML)

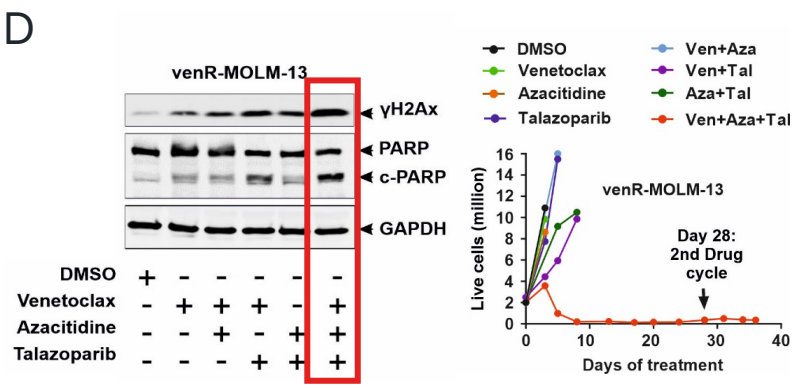
About AML

- Highly aggressive blood cancer
- Proliferation and accumulation of leukemic blasts
- Combination of venetoclax+azacitidine (ven+aza) has become standard therapy for patients ineligible for chemotherapy.









About PARP1+2

- Crucial in mediating DNA damage repair
- PARP2: essential for the maintenance of normal hematopoiesis
- Clinical use of dual PARP1/2 inhibitors is associated with cytopenias
- PARP1-selective inhibitors retain therapeutic benefit and exhibit a more favourable toxicity profile

Abbreviations:

venR	venetoclax resistant
cPARP	cleaved PARP

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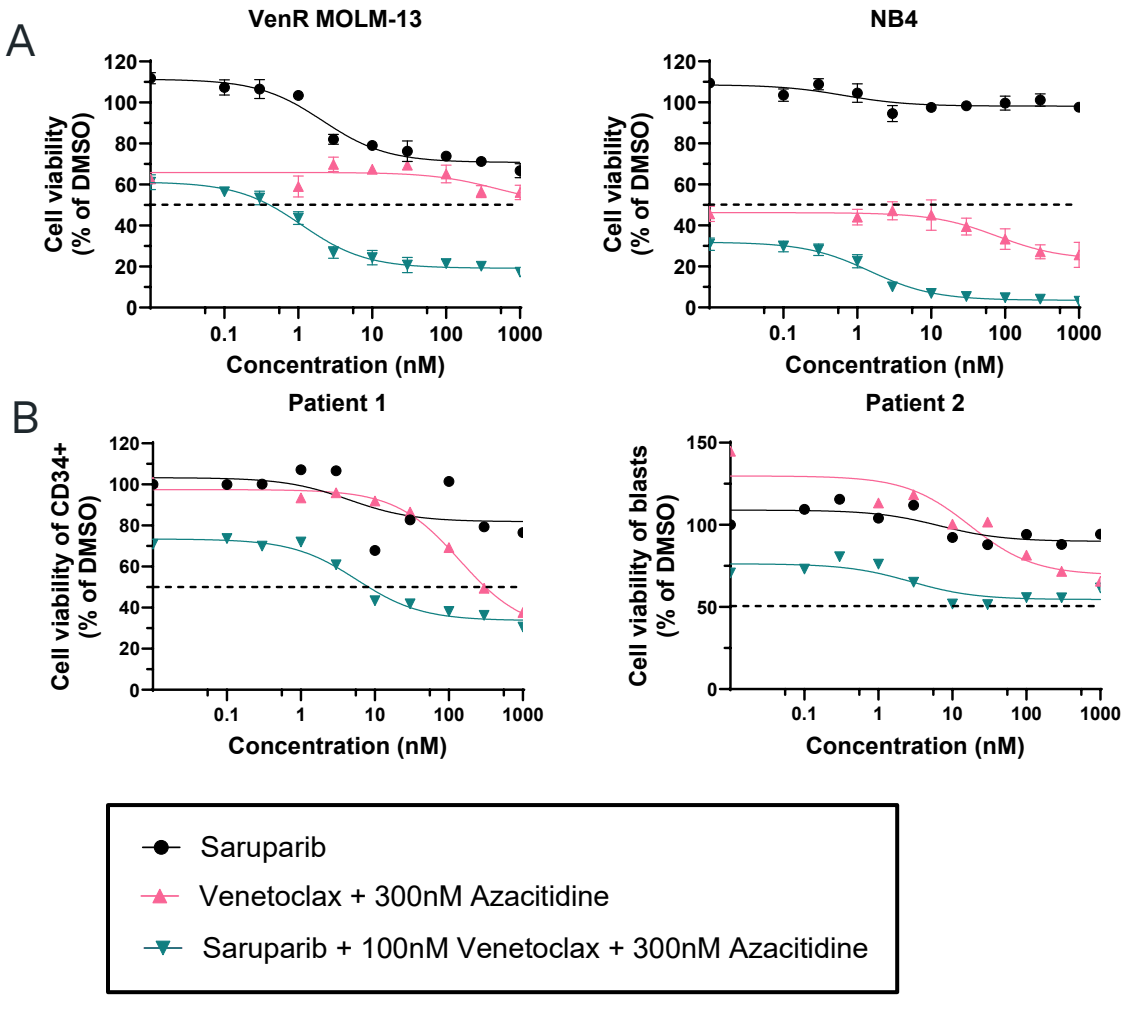
Figures were created with BioRender.com

QUESTION:

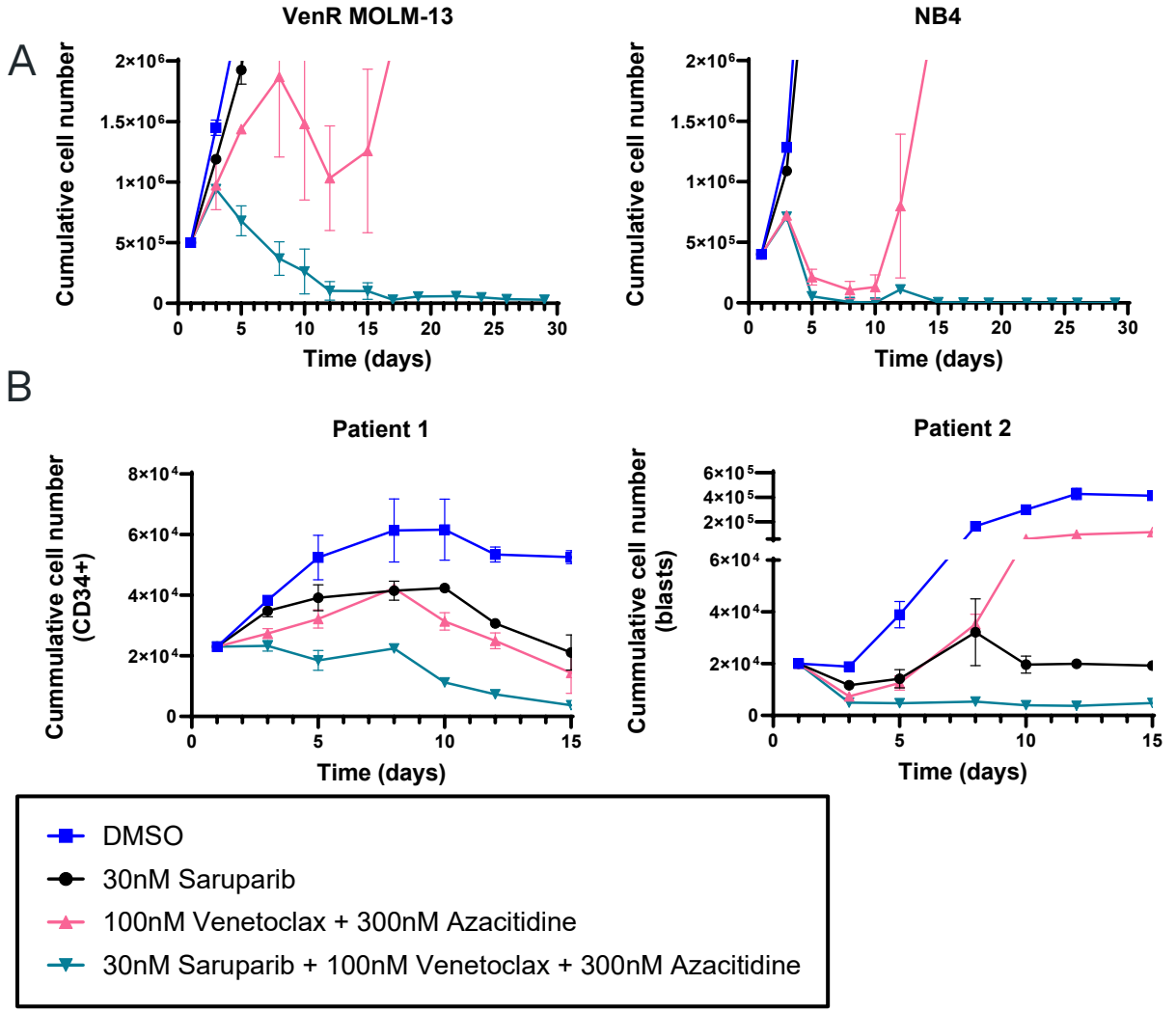
Can combining ven+aza with the PARP1-selective inhibitor saruparib enhance the treatment response in venR AML cell lines and samples from AML patients with a poor or no clinical response to ven+aza therapy?

THE COMBINATION OF SARUPARIB WITH VEN+AZA RESULTS IN ENHANCED CYTOTOXICITY

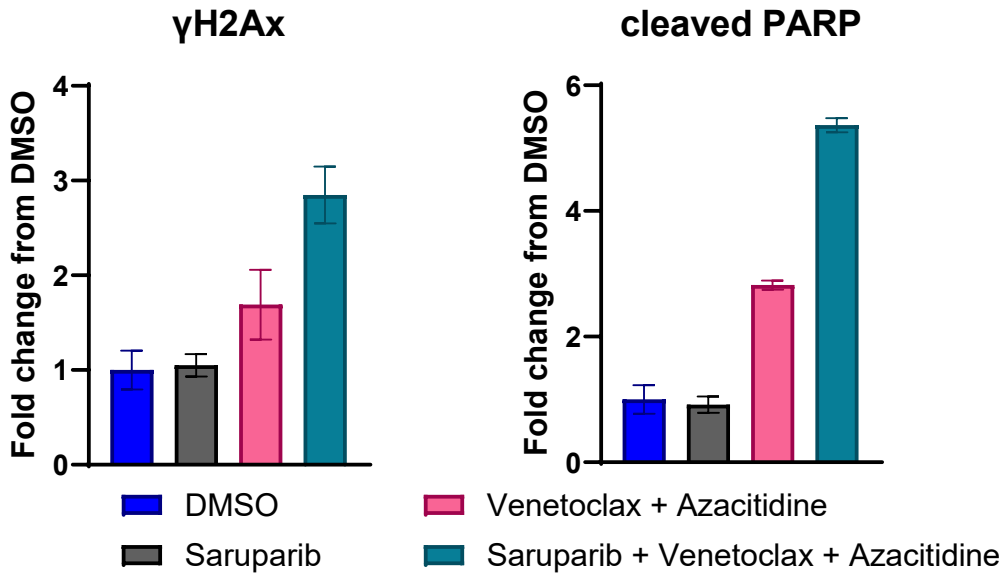
DRUG RESPONSE TESTING



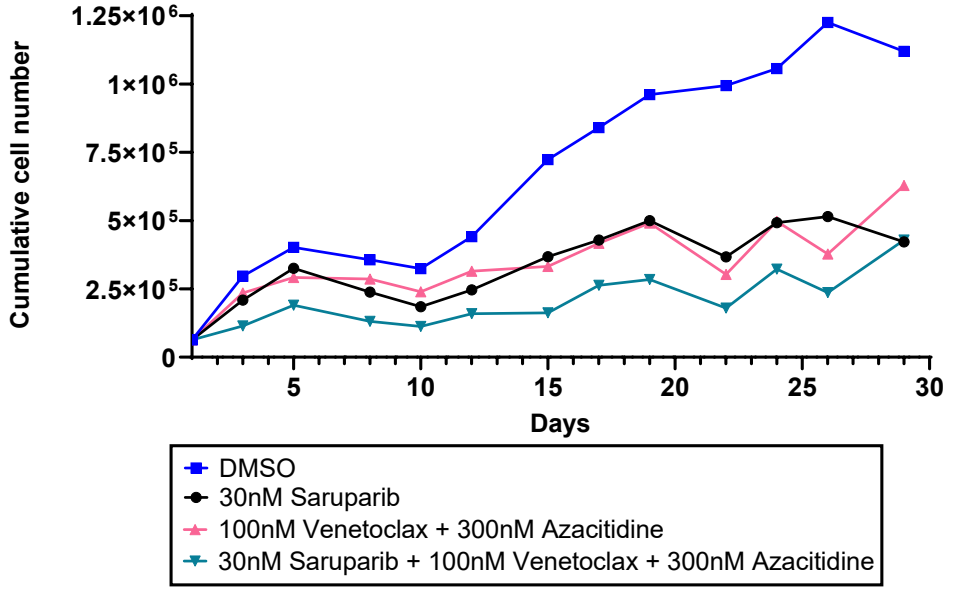
LONG-TERM EXPERIMENTS



THE TRIPLE COMBINATION INDUCES HIGH LEVELS OF DNA DAMAGE AND APOPTOSIS IN VENR AML CELLS



SARUPARIB COMBINED WITH VEN+AZA EXHIBITS MODEST CYTOTOXICITY IN HEALTHY HEMATOPOIETIC PROGENITOR CELLS



CONCLUSION:

- The selective PARP1 inhibitor saruparib combined with ven+aza enhances cytotoxicity *in vitro* in venR AML cell lines and patient samples
- This tailored approach addresses a major clinical challenge by optimizing therapeutic efficacy where previous treatments have failed and may improve therapy outcomes in a population with limited options.

ACKNOWLEDGEMENTS

Mika Kontro
Heikki Kuusanmäki
Mahesh Tambe
Caroline A. Heckman

Patients

Justinas Daraskevicius
Emelie Jansson
Héloïse Pichard
Kim Theilgaard-Mönch
Krister Wennerberg

DISCLOSURES/FUNDING

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No. 101034291 (DISCOVER).

This work was funded by

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Poster #34

Wennerberg Group @ BRIC

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