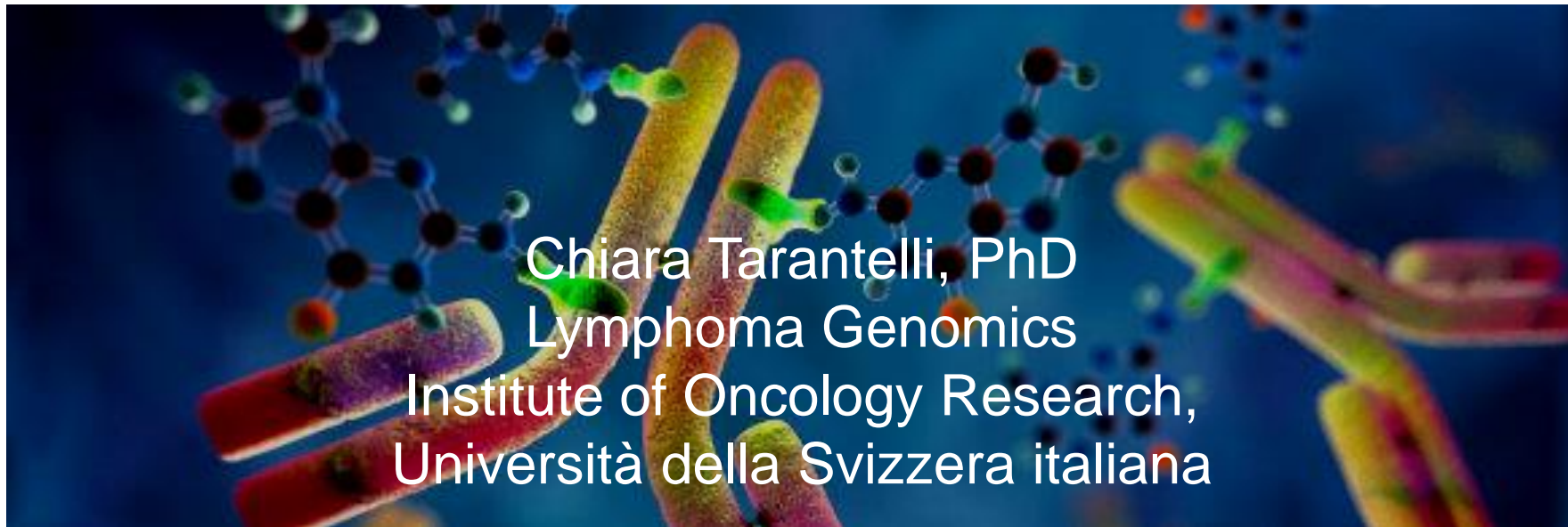
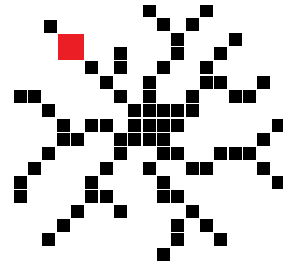


**The antibody-drug conjugate (ADC)  
loncastuximab tesirine (ADCT-402) targeting  
CD19 shows strong *in vitro* anti-lymphoma activity  
both as single agents and in combination**

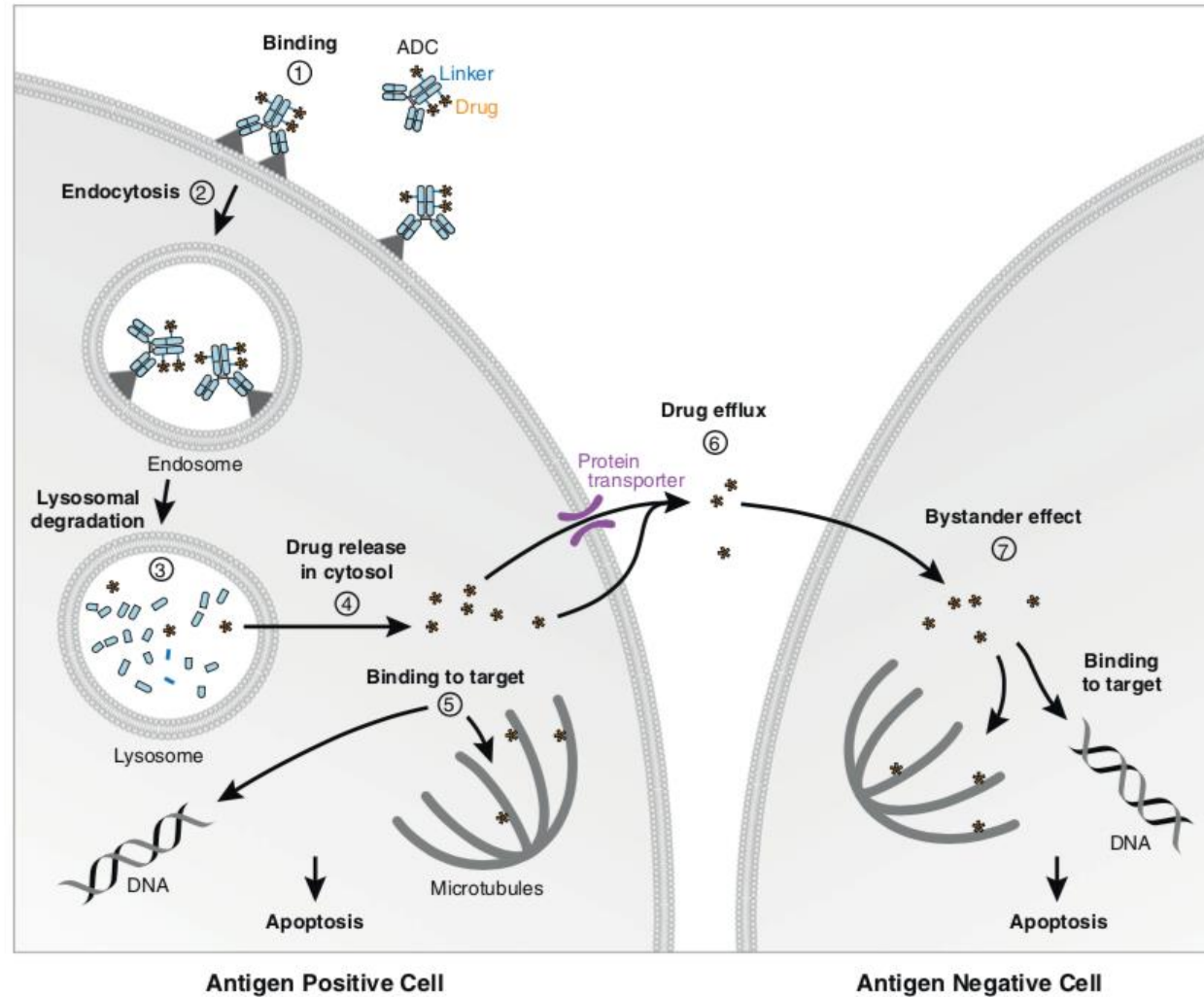




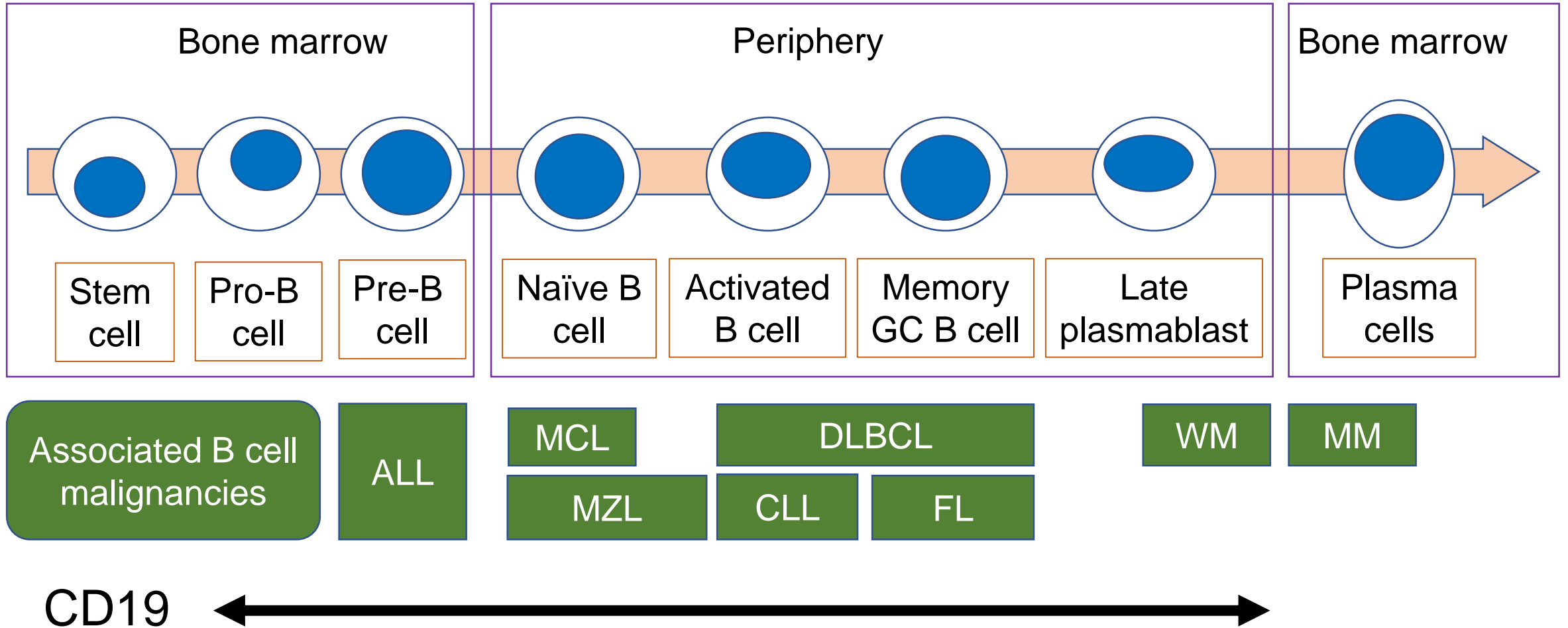
## Conflict of Interest Disclosure – Chiara Tarantelli, Presentation Nr. 84

- Employment or leadership position:
- Consultant or advisory role: N/A
- Stock ownership: N/A
- Honoraria: N/A
- Research funding: ADC Therapeutics
- Other remuneration: N/A

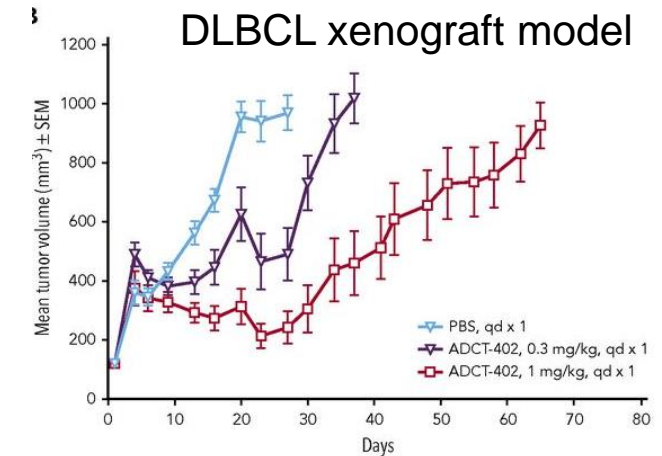
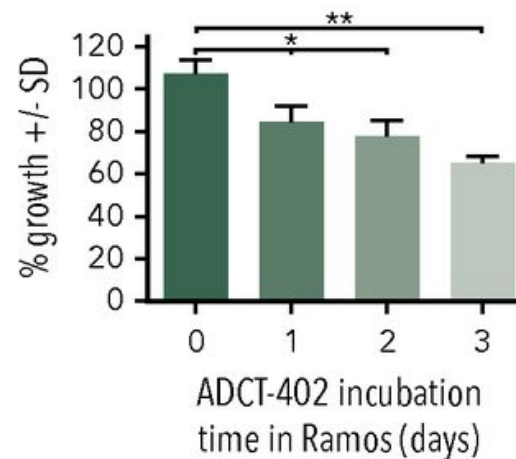
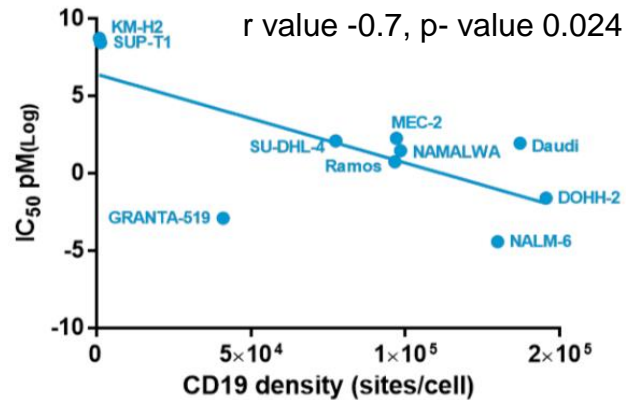
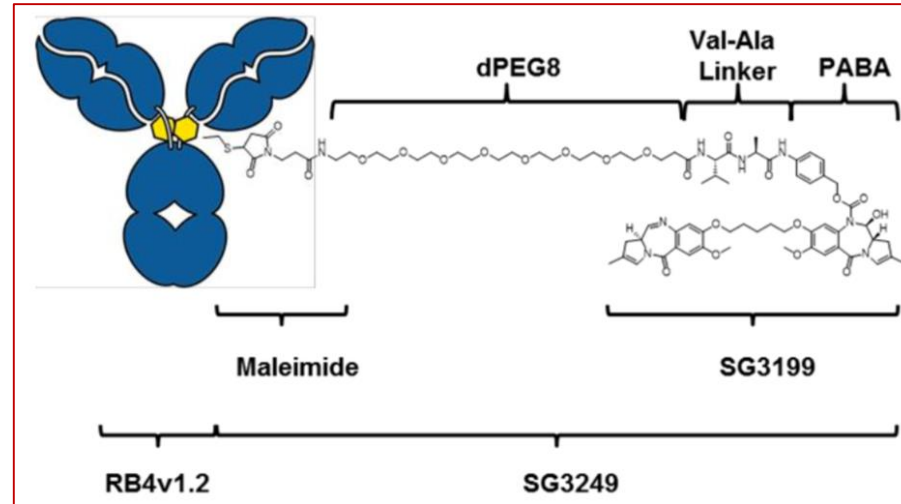
# Antibody Drug Conjugate (ADC)



# CD19: expressed across all B cell development stages

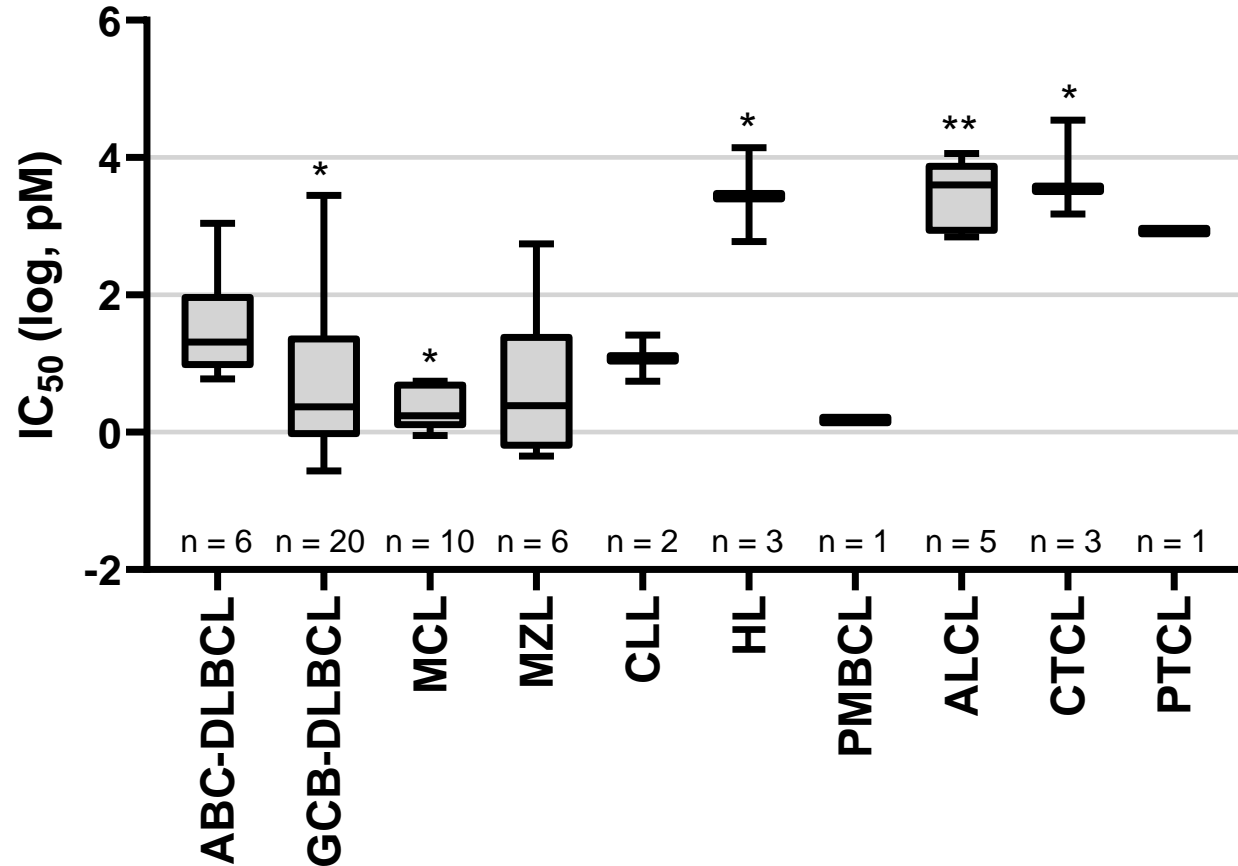


# Loncastuximab tesirine (ADCT-402) is a new anti-CD19 ADC active against hematological malignancies



NCT number	Study title	Phase	Status
NCT02669017	Dose-escalation Study to Evaluate the Tolerability, Safety, Pharmacokinetics, and Antitumor Activity of ADCT-402 in Patients With Relapsed or Refractory B-NHL	Phase 1	Completed *
NCT03589469	Study to Evaluate the Efficacy and Safety of Loncastuximab Tesirine in Patients With Relapsed or Refractory DLBCL	Phase 2	Recruiting
NCT03684694	Safety and Antitumor Activity Study of Loncastuximab Tesirine + Ibrutinib in DLBCL or MCL	Phase 1	Recruiting
NCT03685344	Safety and Antitumor Activity Study of Loncastuximab Tesirine and Durvalumab in DLBCL, MCL, or FL	Phase 1	Recruiting

\* Oral (abstract 054) by J. Radford approximately one hour ago also here at the ICML

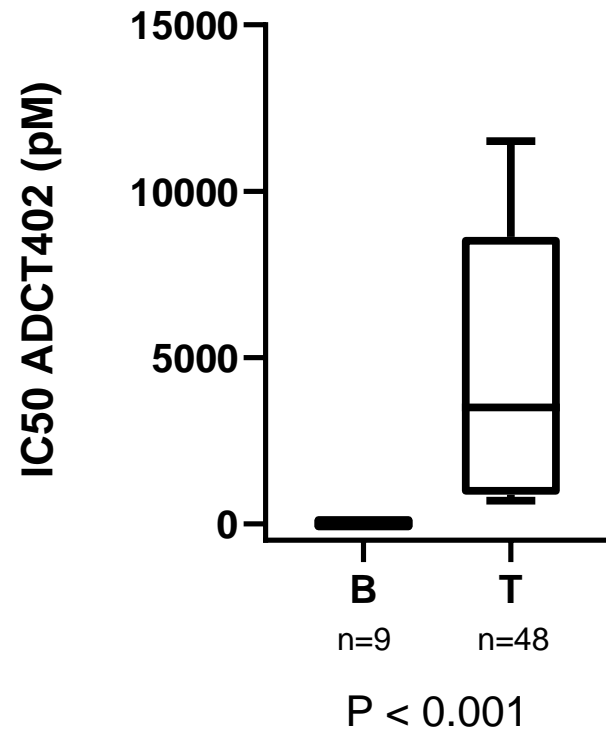


	Number of cell lines	Median IC <sub>50</sub> (log, pM)	95% CI
ABC-DLBCL	6	1.3	0.8-3
GCB-DLBCL	20	0.4	0.1-1.1
MCL	10	0.2	0.0-0.7
MZL	6	0.4	-0.3-2.7
CLL	2	1.8	0.7-1.4
HL	3	3.4	2.8-4.1
PMBCL	1	0.1	n/a
ALCL	5	3.6	2.8-4
CTCL	3	3.5	3.2-4.5
PTCL	1	2.9	n/a

MTT proliferation assay and IC<sub>50</sub> calculation on cell lines exposed (96h) to increasing ADCT-402 concentrations

\*, P<0.05; \*\*, P<0.01





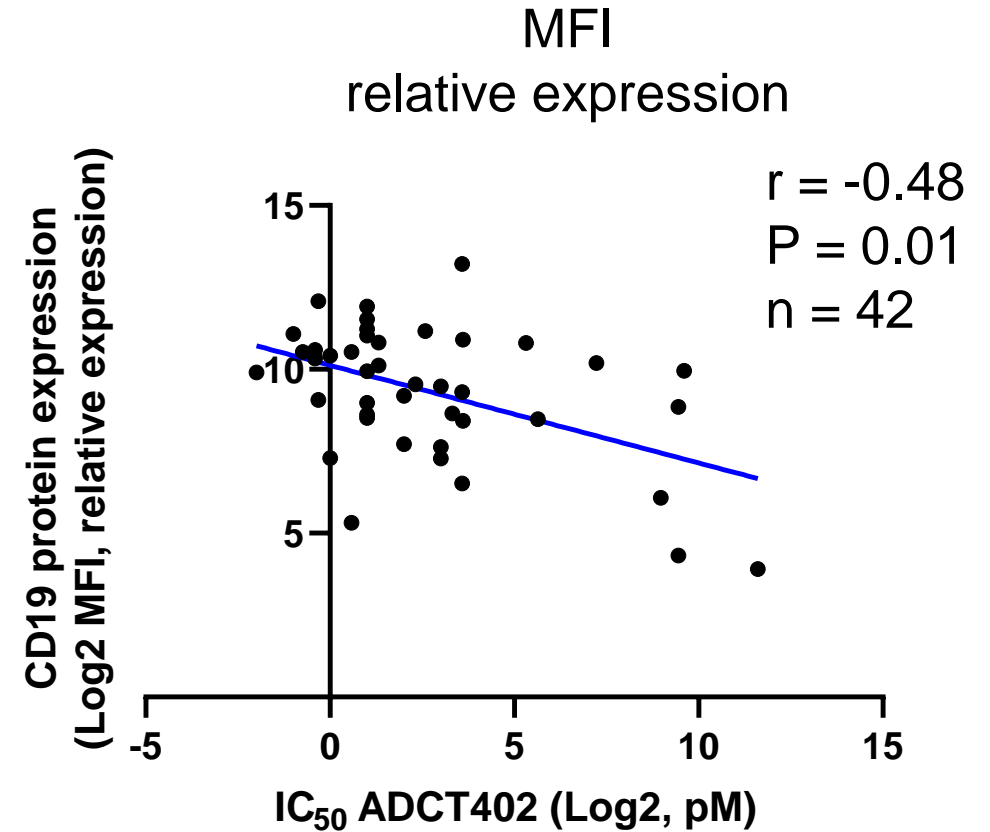
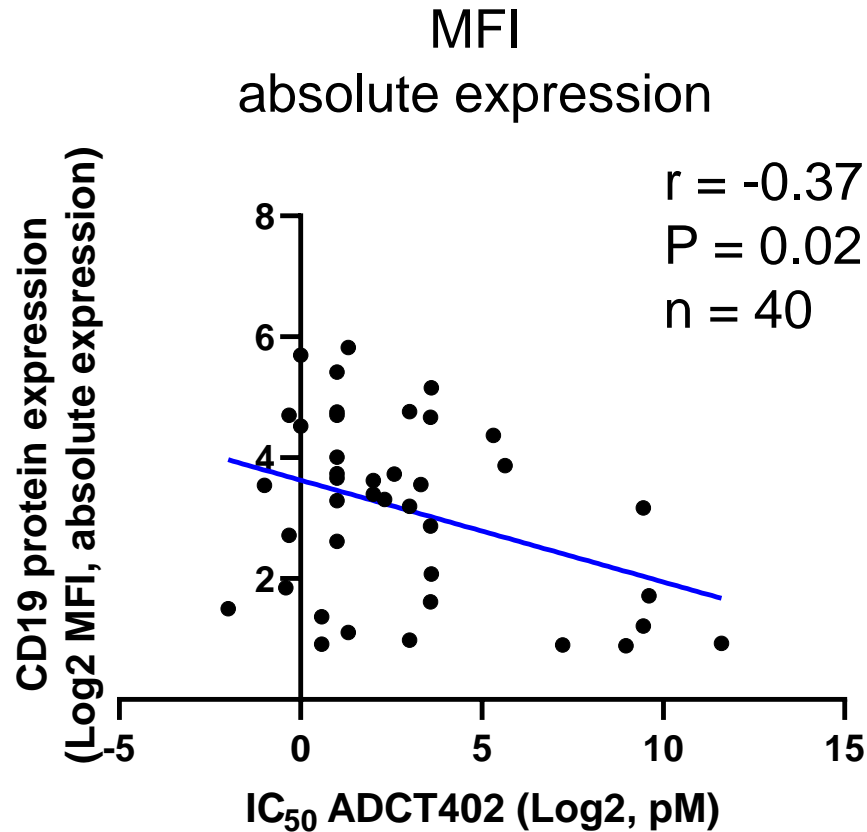
**B-cell lymphoma** (n=48)  
median IC50=4 pM (95%C.I, 2-10 pM)

**T-cell lymphoma** (n=9)  
median IC50=3.5 nM (95%C.I, 0.8-11 nM)

MTT proliferation assay and IC50 calculation on cell lines exposed (96h) to increasing ADCT-402 concentrations

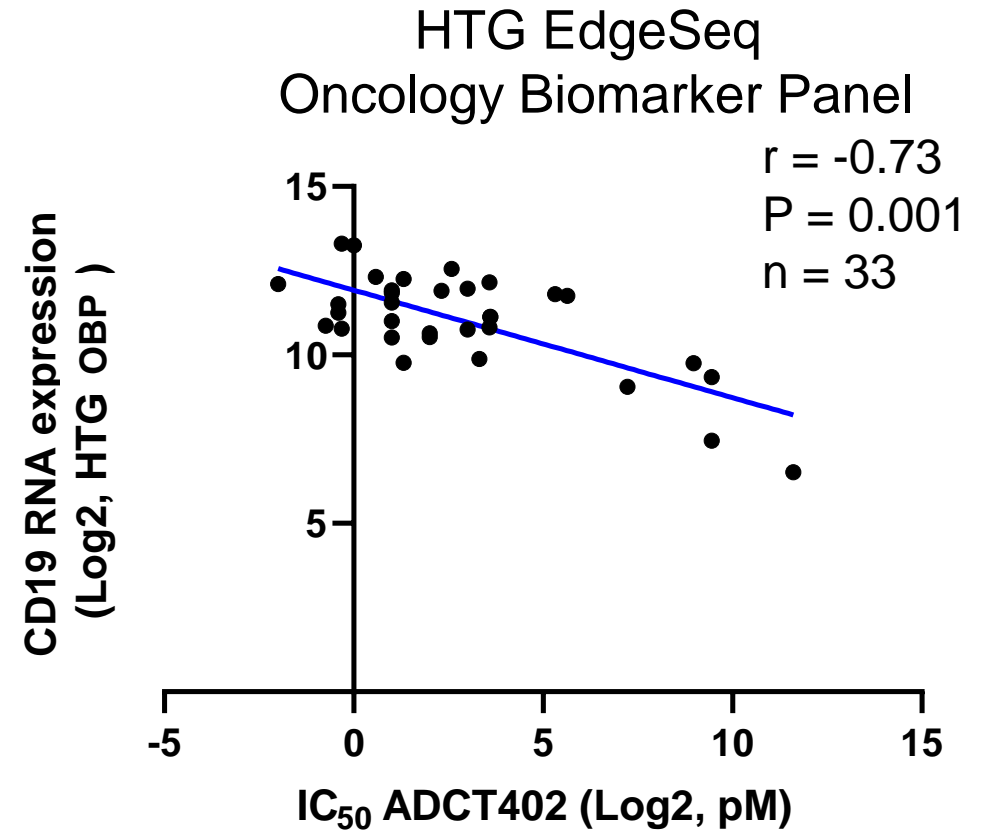
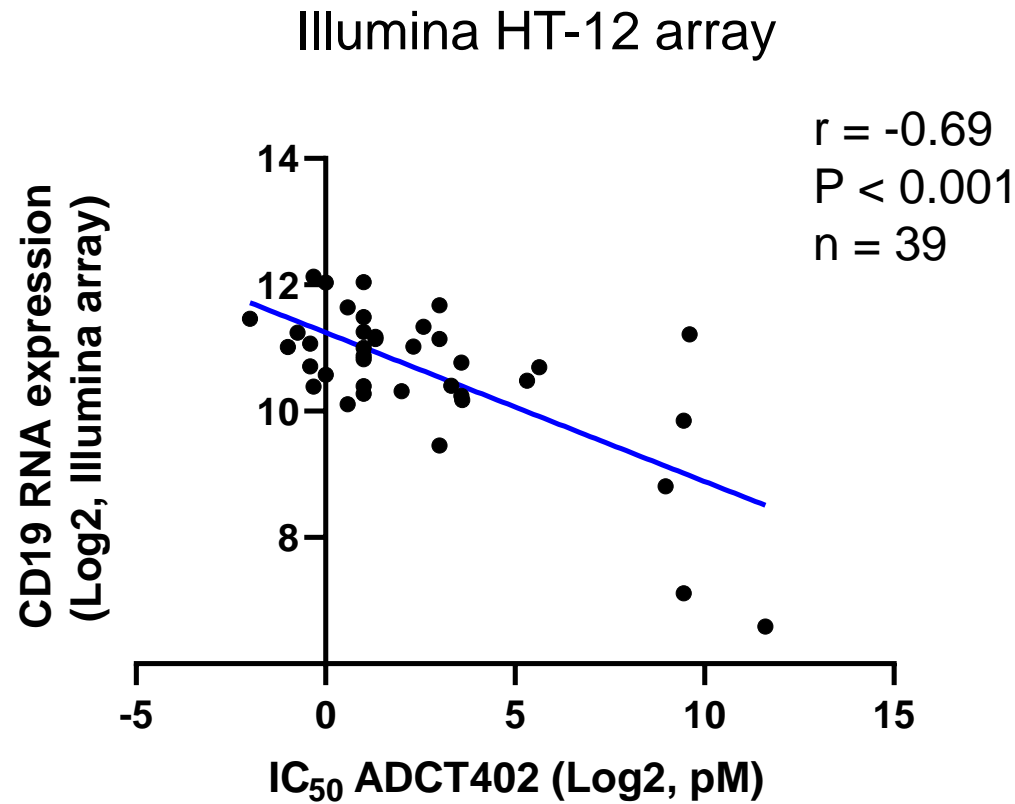


# ADCT-402 *in vitro* activity correlates with CD19 surface protein expression in B cell lines



Pearson correlation (r)

# ADCT-402 *in vitro* activity correlates with CD19 RNA levels in B cell lines



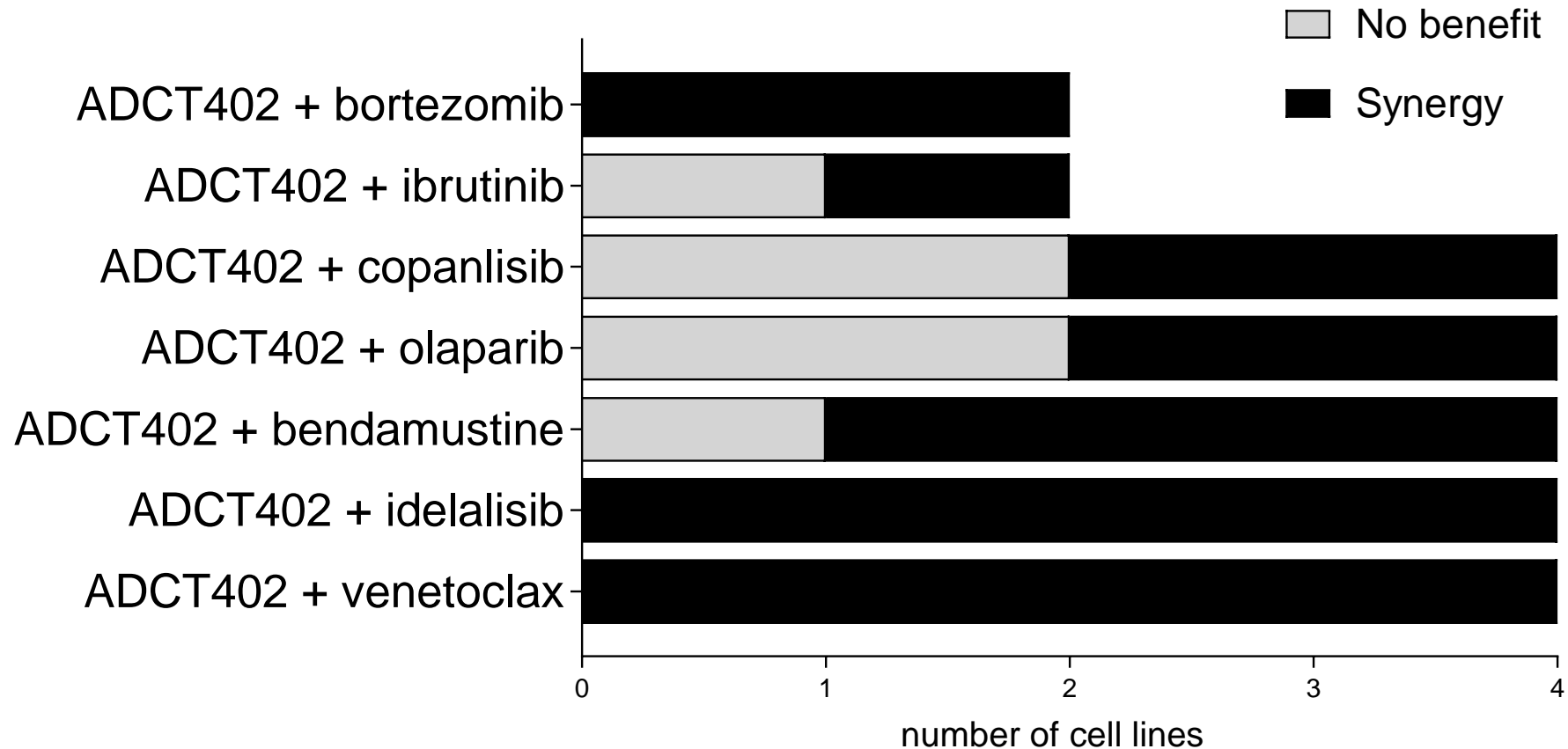
Pearson correlation (r)

Second drug	Target / MOA
venetoclax	BCL2 inhibitor
Ibrutinib *	BTK inhibitor
bendamustine	Chemotherapy agent
lenalidomide	Immunomodulator
copanlisib	PI3K inhibitor
idelalisib	PI3K $\delta$ inhibitor
olaparib	PARP inhibitor
bortezomib *	Proteasome inhibitor

\* ABC only

MTT proliferation assay, 96h, 2 ABC – 2 GCB DLBCL cell lines  
Synergy assessed by Chou-Talalay combination index (CI)  
synergism  $CI < 0.9$ , additive  $CI = 0.9 - 1.1$ , antagonism/no benefit  $CI > 1.1$

# ADCT-402: best synergism with venetoclax, idelalisib and bendamustine



MTT proliferation assay, 96h, 2 ABC – 2 GCB DLBCL cell lines  
 Synergy assessed by Chou-Talalay combination index (CI)  
 synergism  $CI < 0.9$ , additive  $CI = 0.9 - 1.1$ , antagonism/no benefit  $CI > 1.1$

# Conclusions

- ADCT-402 is strongly active *in vitro* in a wide panel of lymphoma cell lines
- ADCT-402 *in vitro* activity correlates with CD19 expression at protein and RNA level
- The results support the currently on-going clinical studies in relapsed/refractory DLBCL
- The novel combination data provide rational for further clinical development, such as combination with venetoclax, idelalisib and bendamustine.

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