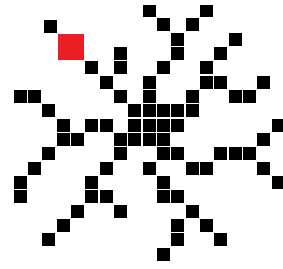


**The antibody-drug conjugate (ADC)  
loncastuximab tesirine (ADCT-402) targeting  
CD19 shows strong *in vitro* anti-lymphoma activity  
both as single agents and in combination**

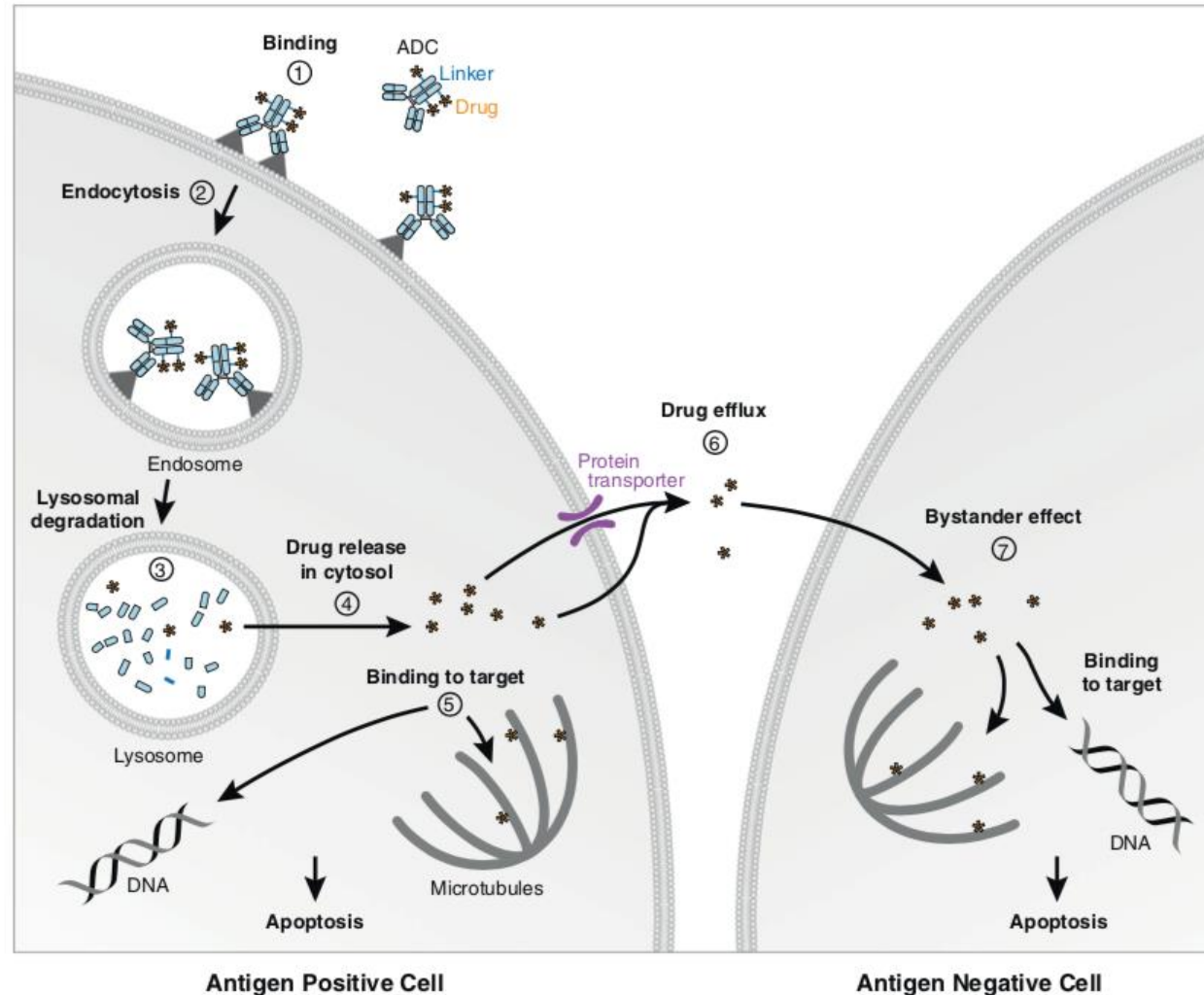




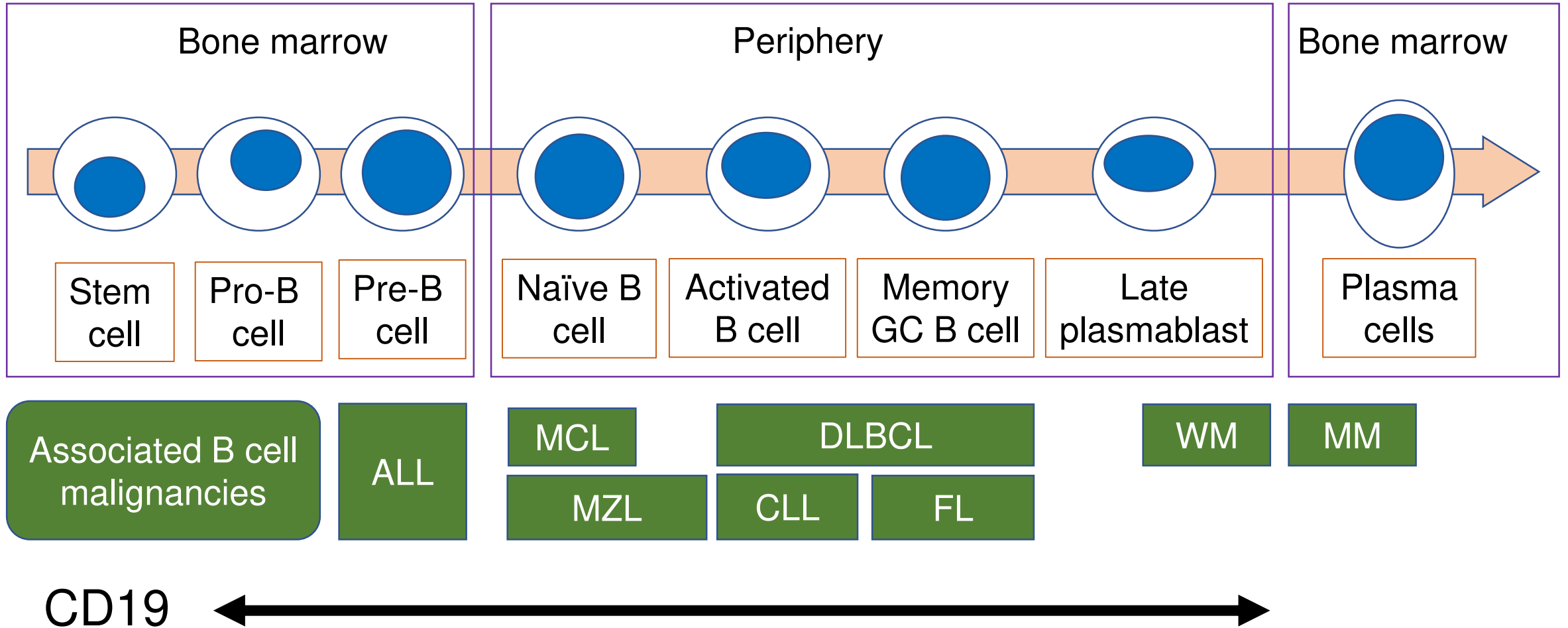
## Conflict of Interest Disclosure – Chiara Tarantelli, Presentation Nr. 84

- 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

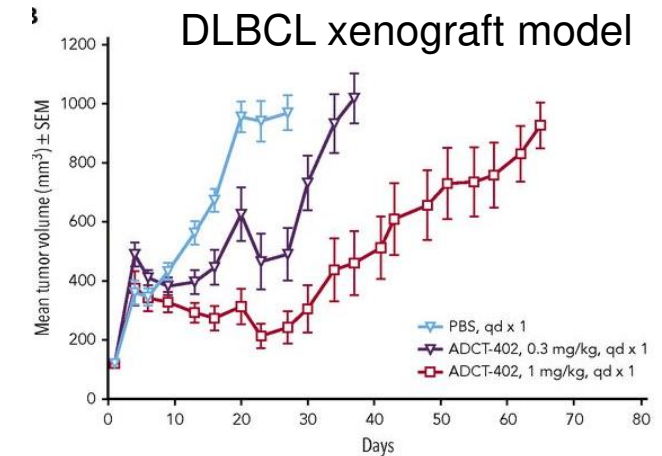
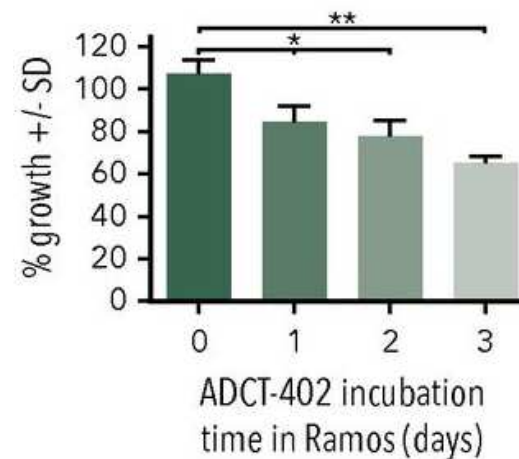
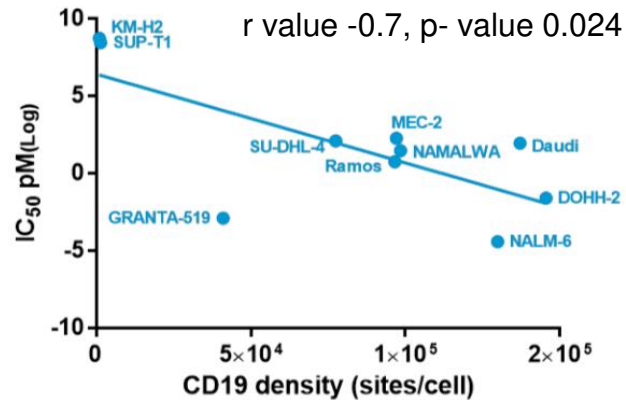
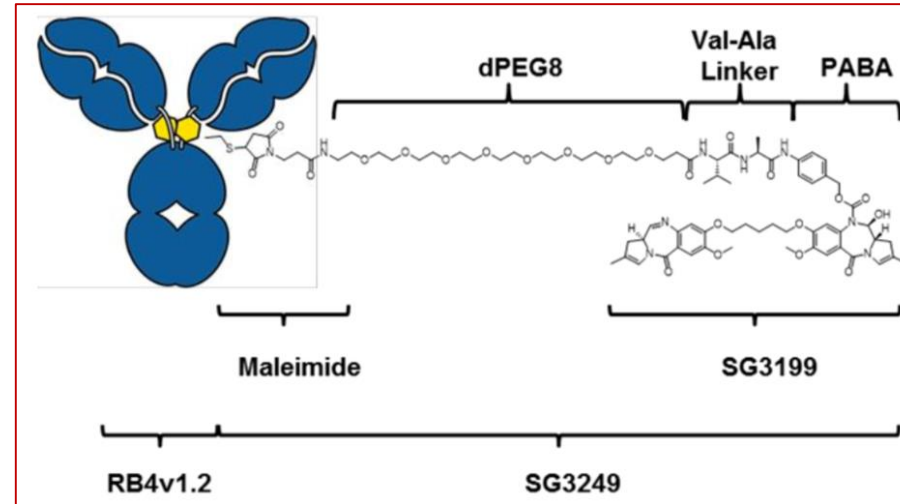
# Antibody Drug Conjugate (ADC)



# CD19: expressed across all B cell development stages

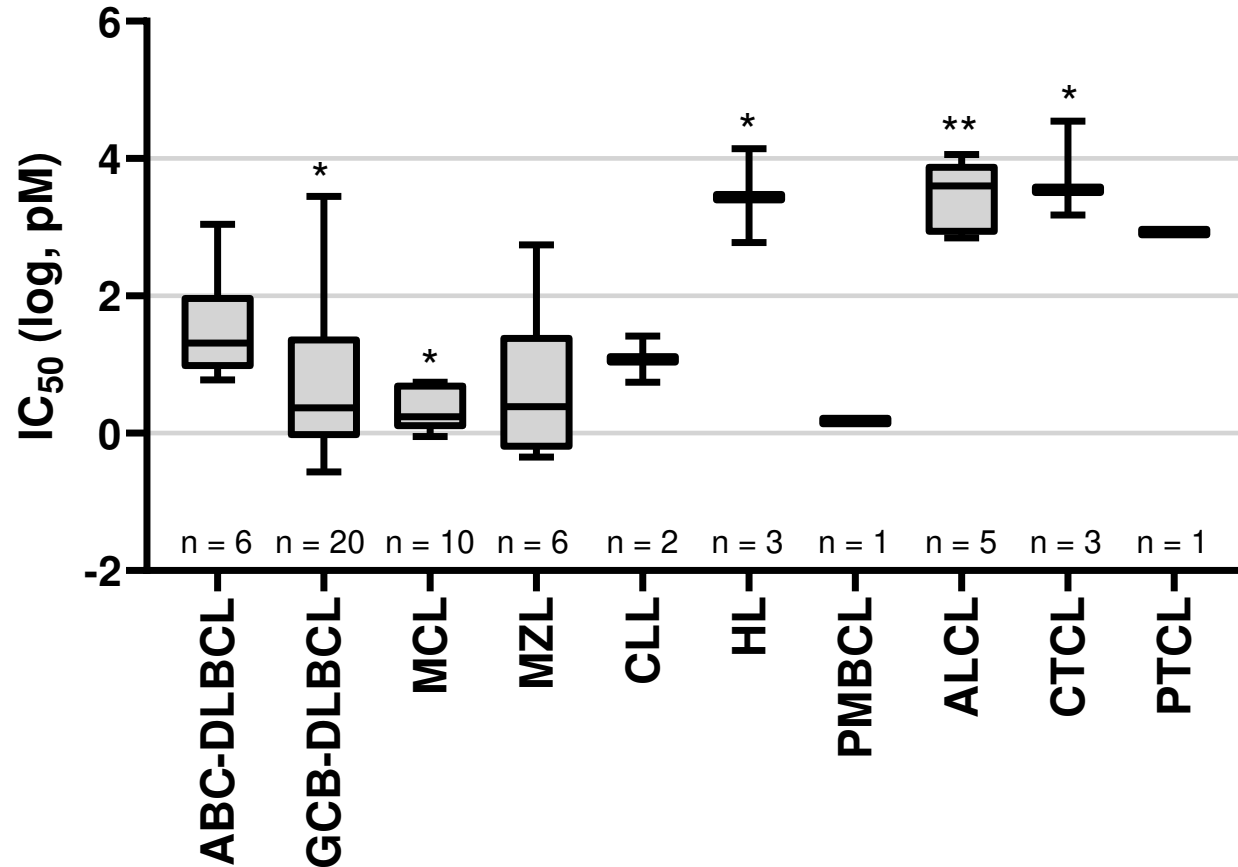


# Loncastuximab tesirine (ADCT-402) is a new anti-CD19 ADC active against hematological malignancies



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

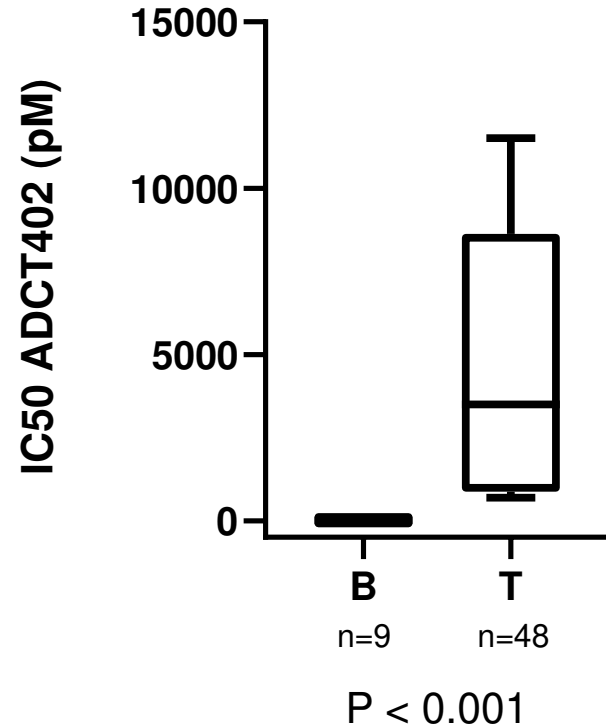
\* Oral (abstract 054) by J. Radford approximately one hour ago also here at the ICML



	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



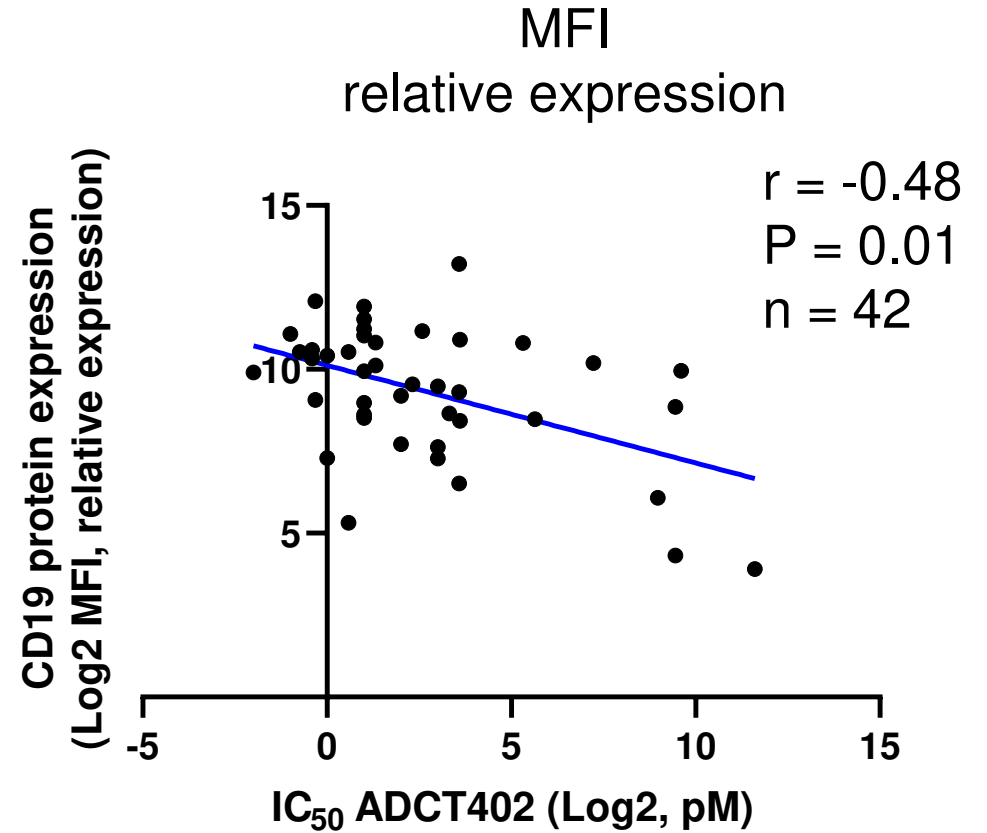
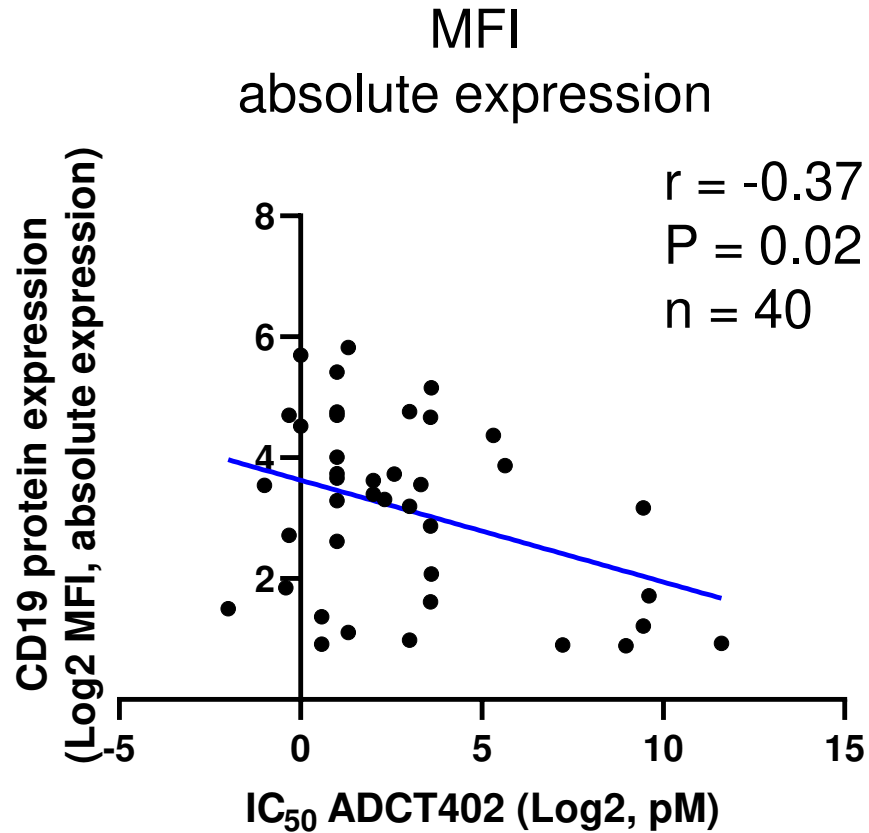
**B-cell lymphoma** (n=48)  
median IC50=4 pM (95%C.I, 2-10 pM)

**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

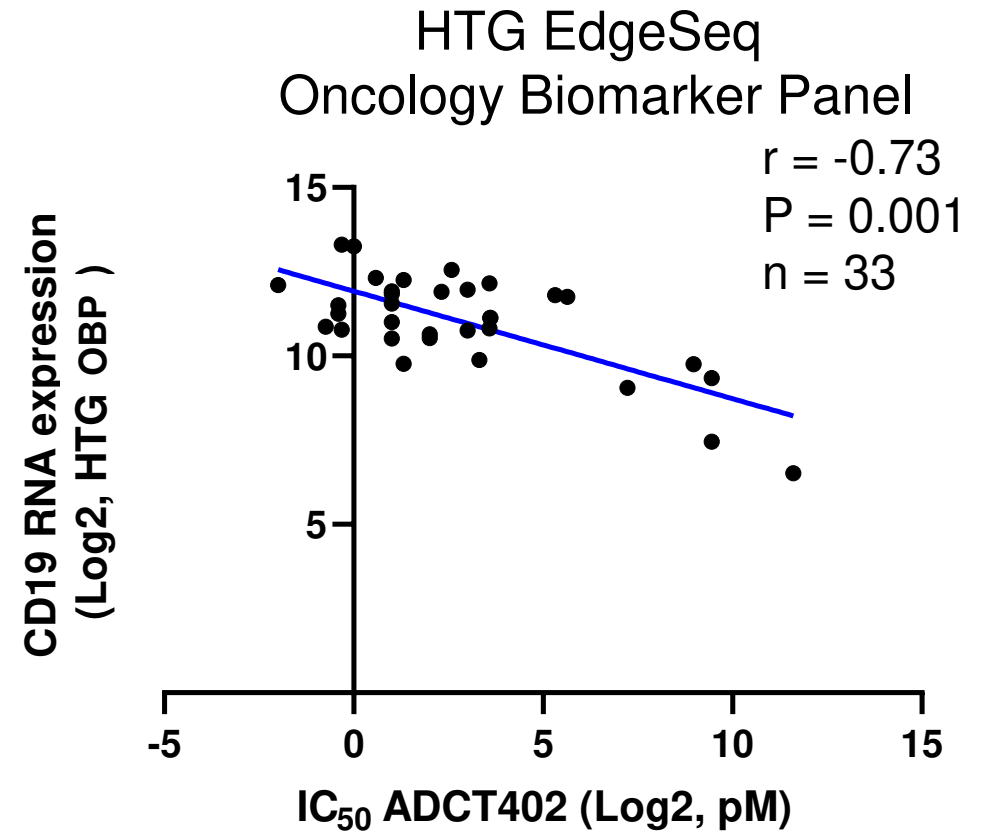
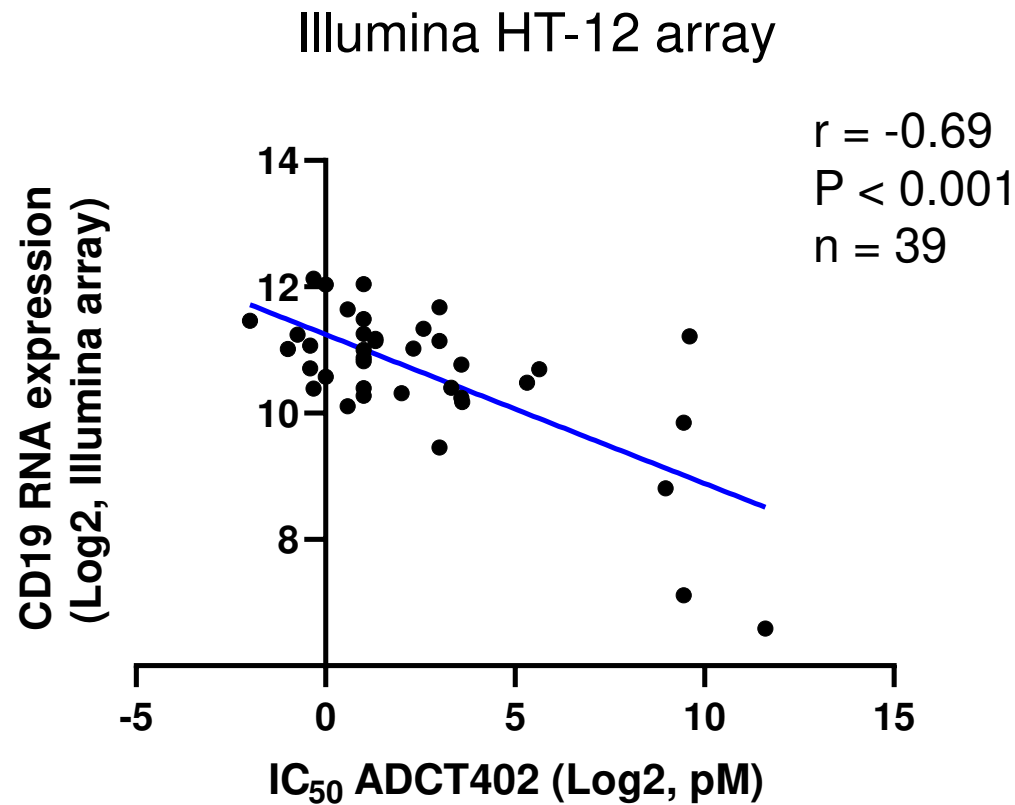


# ADCT-402 *in vitro* activity correlates with CD19 surface protein expression in B cell lines



Pearson correlation (r)

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



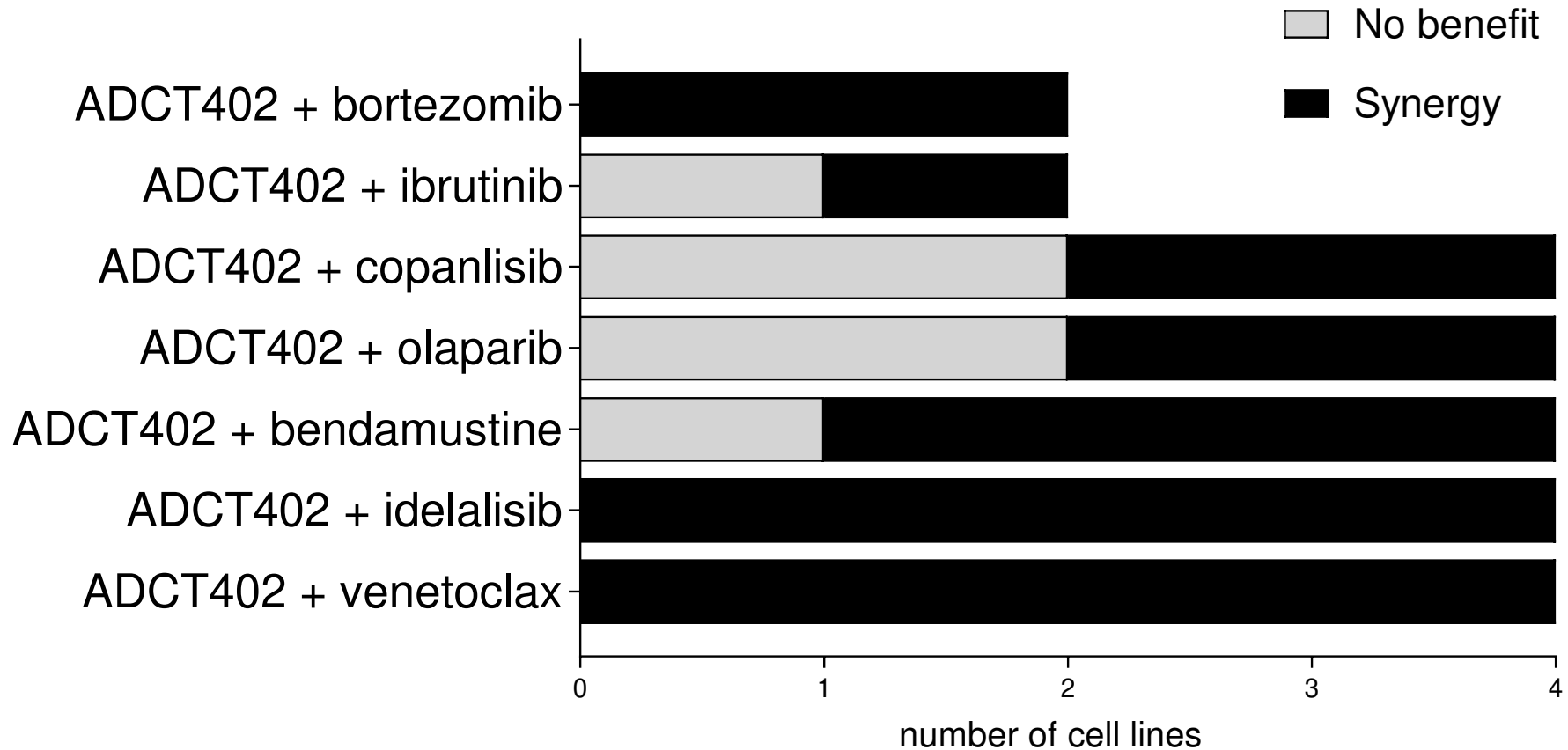
Pearson correlation (r)

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.

# Acknowledgments

Lymphoma Genomics, IOR Institute of Oncology Research,  
Università della Svizzera italiana, Bellinzona, Switzerland



Francesco Bertoni  
Eugenio Gaudio  
Filippo Spriano  
Gaetanina Golino  
Lorenzo Scalise  
Luciano Cascione

IOSI Oncology Institute of Southern Switzerland,  
Bellinzona, Switzerland



Emanuele Zucca  
Anastasios Stathis

ADC Therapeutics (UK) Ltd., London, UK



Francesca Zammarchi  
Patrick H. van Berkel

