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LIS22: An Effective Multimodal Polyclonal Antibody targeting T-Cell Malignancies

Oral presentation
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XENOTHERA

Conflicts of Interest Disclosure

XENOTHERA:
Employee and shareholder

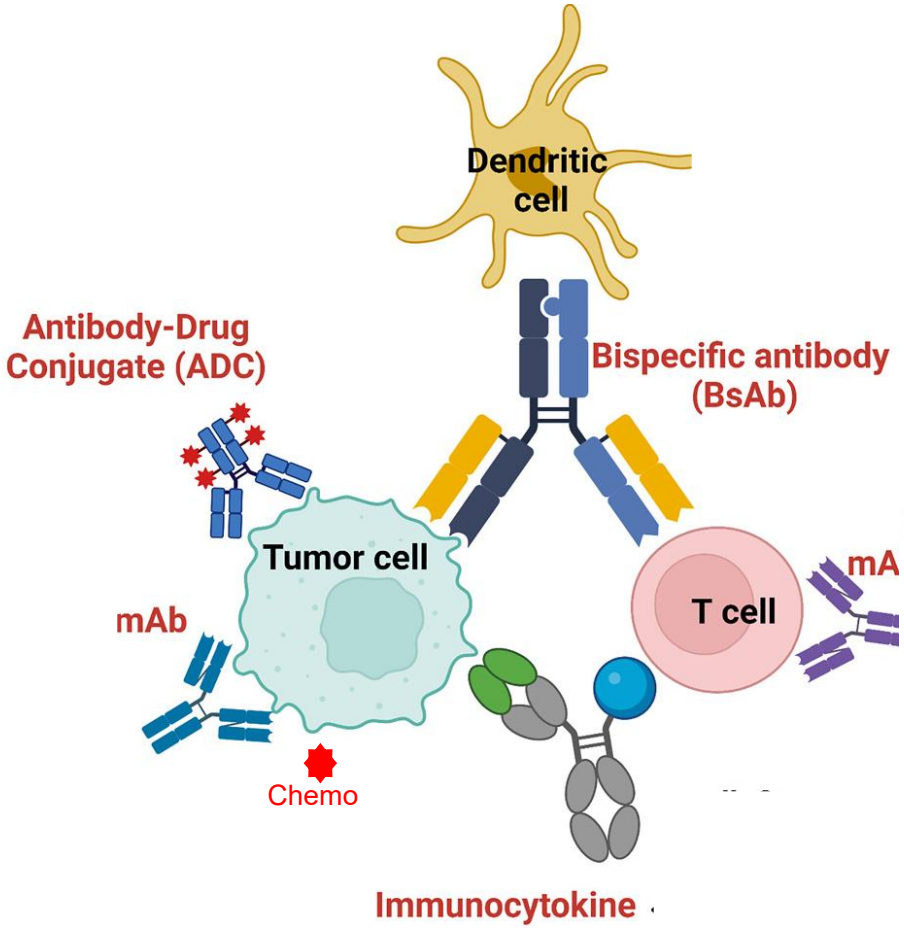
Cancer Treatment: New Horizon

Move from empirical combination to smart combination: multitarget anticancer agents

Past

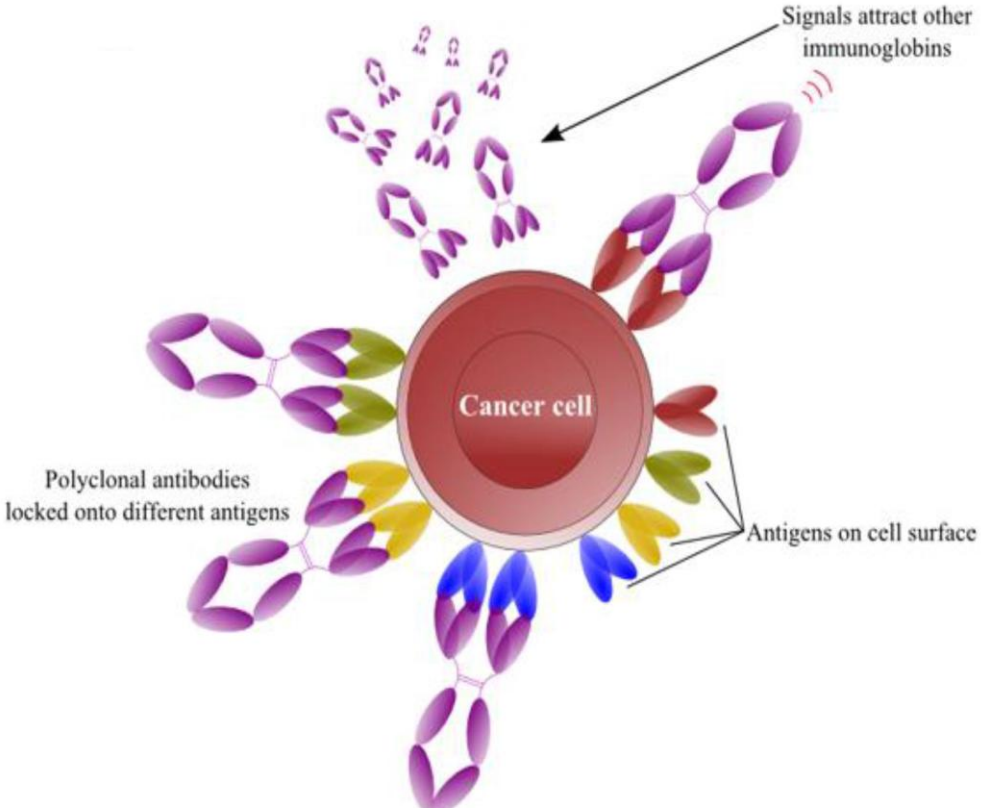
Chemotherapy Cocktails

Present



(Liu and Chen., 2022)

Future?



Schema from Saeed et al., 2017

Multispecific Polyclonal Antibodies will be the next?

Confidential

Why multitarget polyclonal antibodies can be a relevant therapeutical approach against T cell lymphoma ?

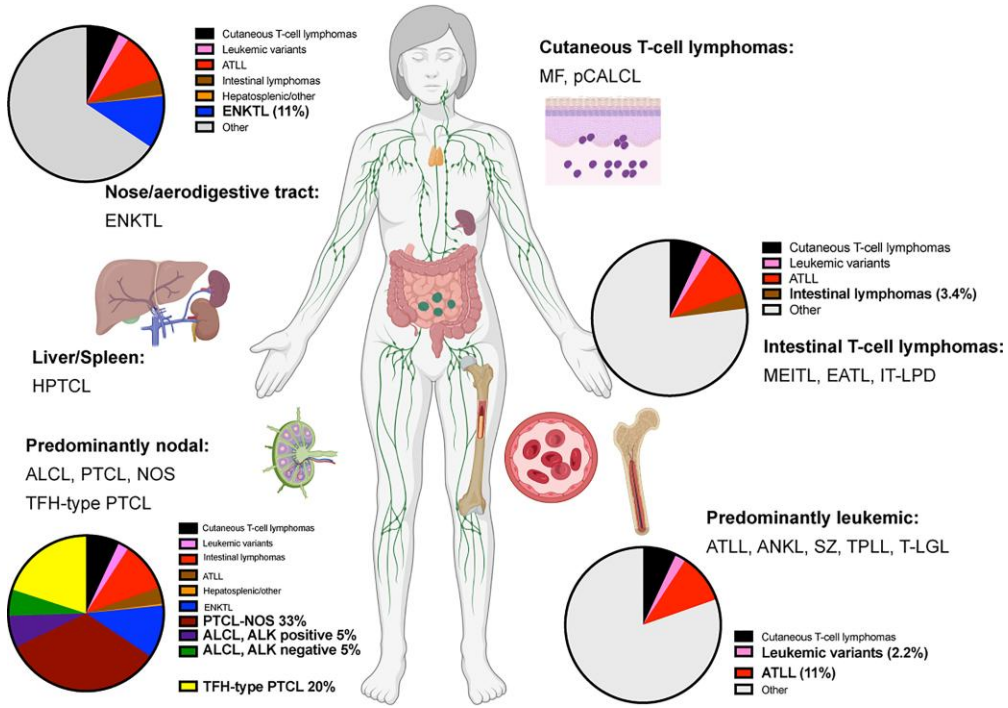
Peripheral T-Cell Lymphoma Background

Peripheral T-cell lymphoma (PTCL) is rare heterogeneous T-cell lymphoma

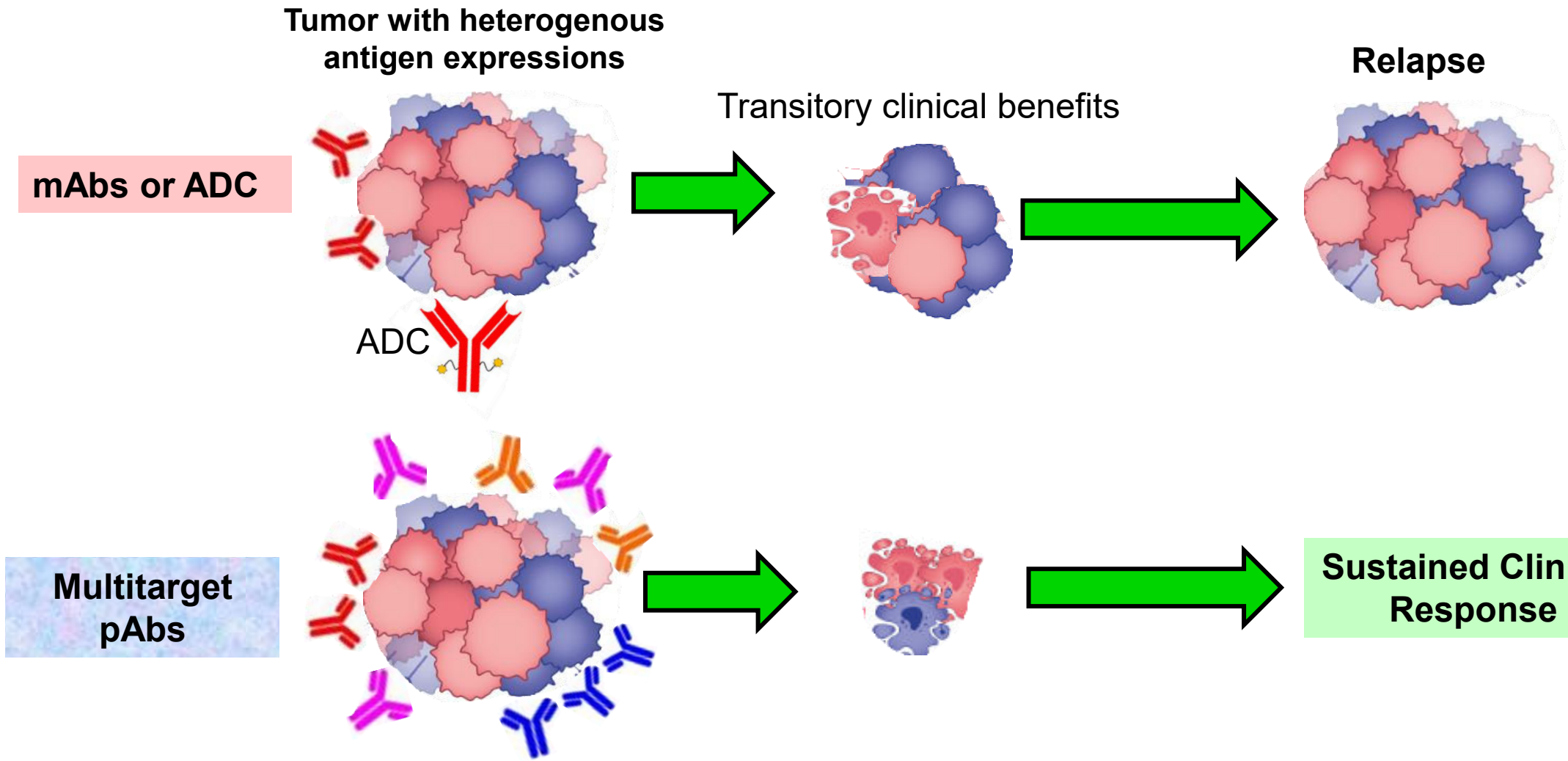
- **High aggressivity and relapse**:

- median overall survival (OS) 6.5 months after relapse
- 5 years OS= 36% after chemotherapy

- **Need for innovative safe and effective therapy to deal with this** heterogenous tumors

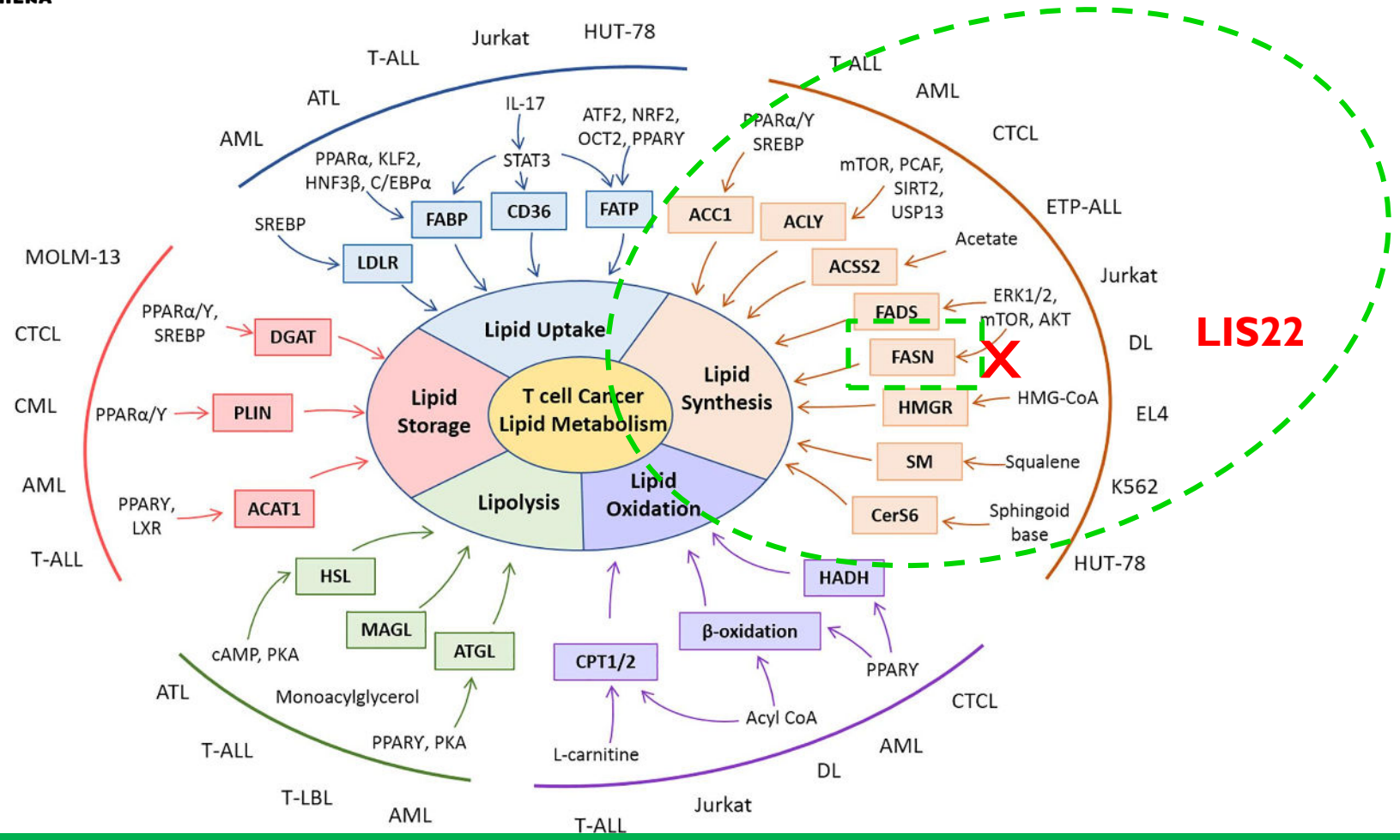


Multitarget Polycolonal Antibodies *vs* mAbs/ADC

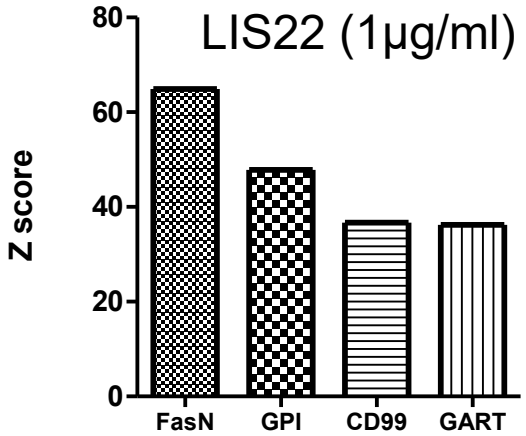


How Does LIS22 act?

LIS22 Targets: tumor metabolic alteration



HuProt™ array (CDI Labs, USA)



LIS22 interacts with several described T cell lymphoma antigens such as FASN, CD99, GPI and GART

Plural mechanisms of action with low immunogenicity

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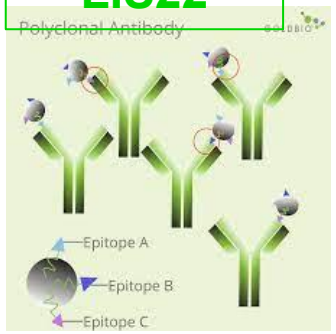
LIS22



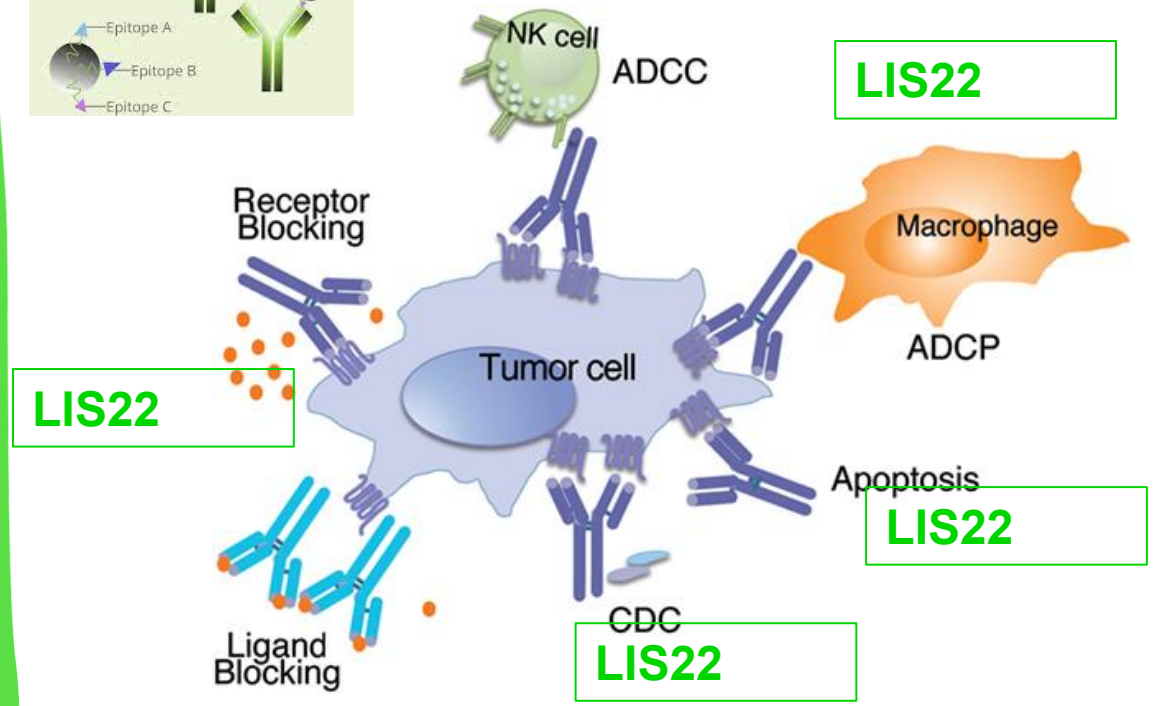
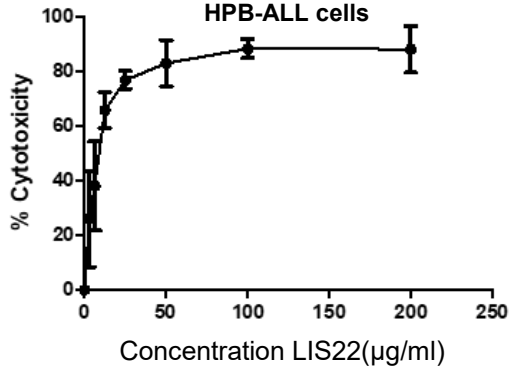
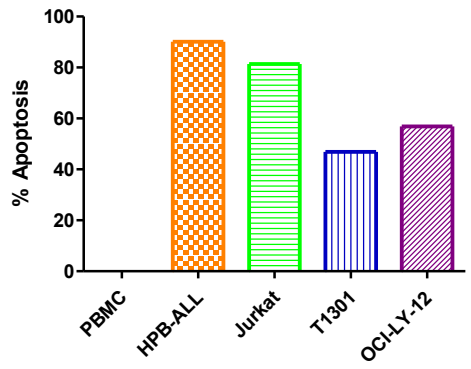


Image: https://www.frontiersin.org/articles/10.3389/fimmu.2017.01804/full

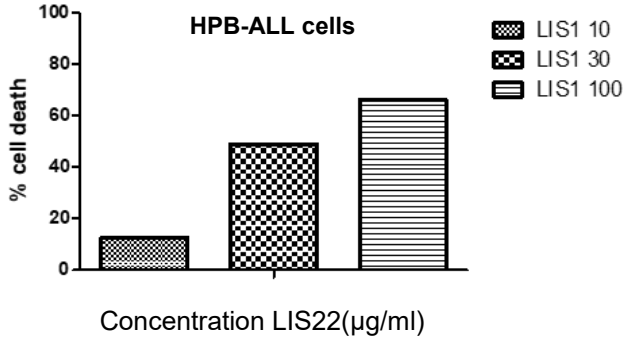
CDC



Apoptosis



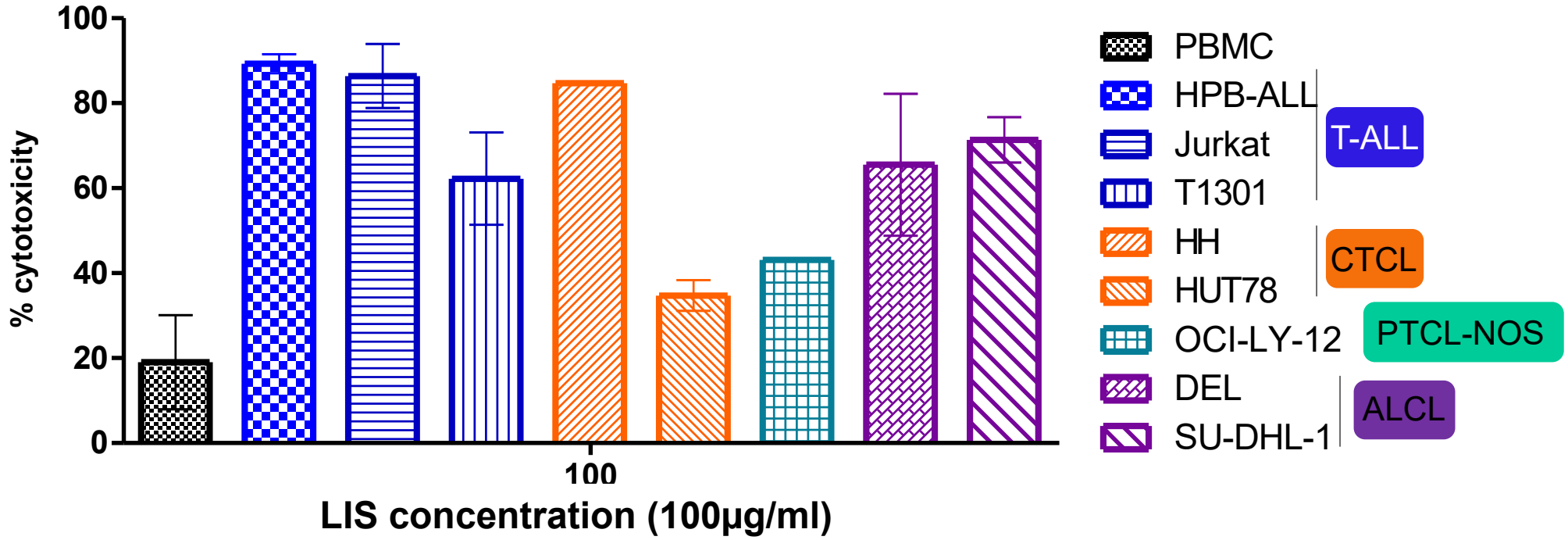
ADCP



LIS22 first in class polyclonal antibody acting selectively against cancer via plural MOA

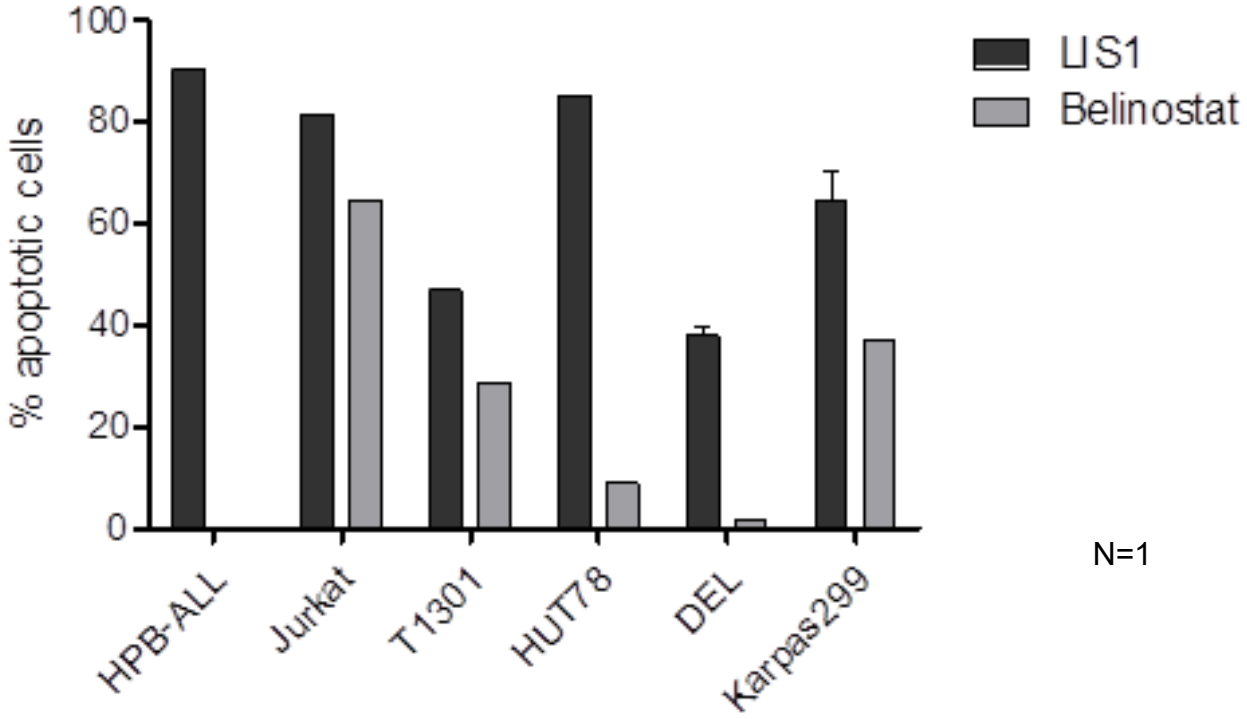
In Vitro Antitumor Activity

Cytotoxicity (CDC) in malignancies T cell lines



High potency against tumor cells without affecting healthy blood cells (PBMC)

LIS22 vs Belinostat Apoptosis activity



N=1

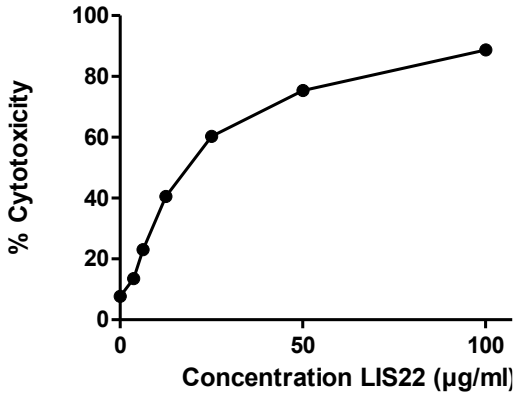
Concentration 100 µg/ml for LIS22 and 100µM for Belinostat

High potency of LIS22 in apoptosis induction assay against almost T cell tumor cells (up to 90%)

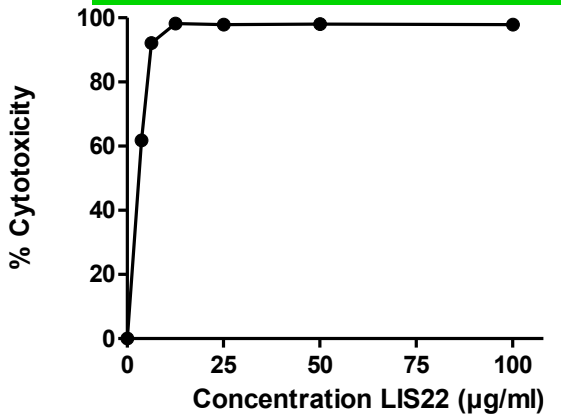
Belinostat (SOC second line) showed lower efficacy on T cell tumors (unsensitive PTCL cell lines such as HUT78 and T ALL HPB-ALL)

LIS22 In vitro activity in PTCL patient tumors: Coll Calym Pr Ortonne

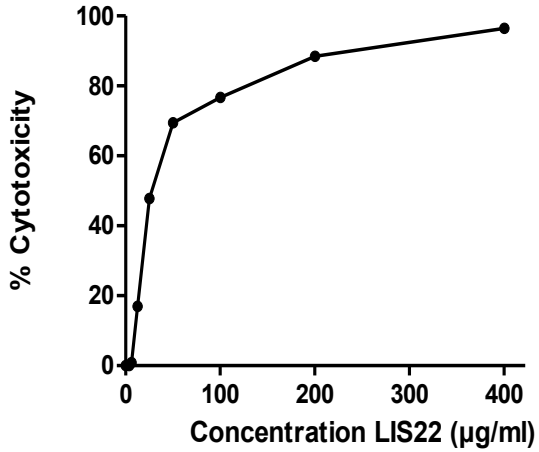
Patient PTCL-NOS 1557



Patient PTCL-NOS 1948



Patient Sezary 1981



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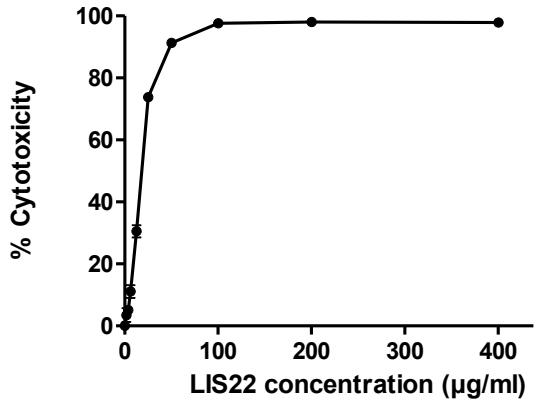
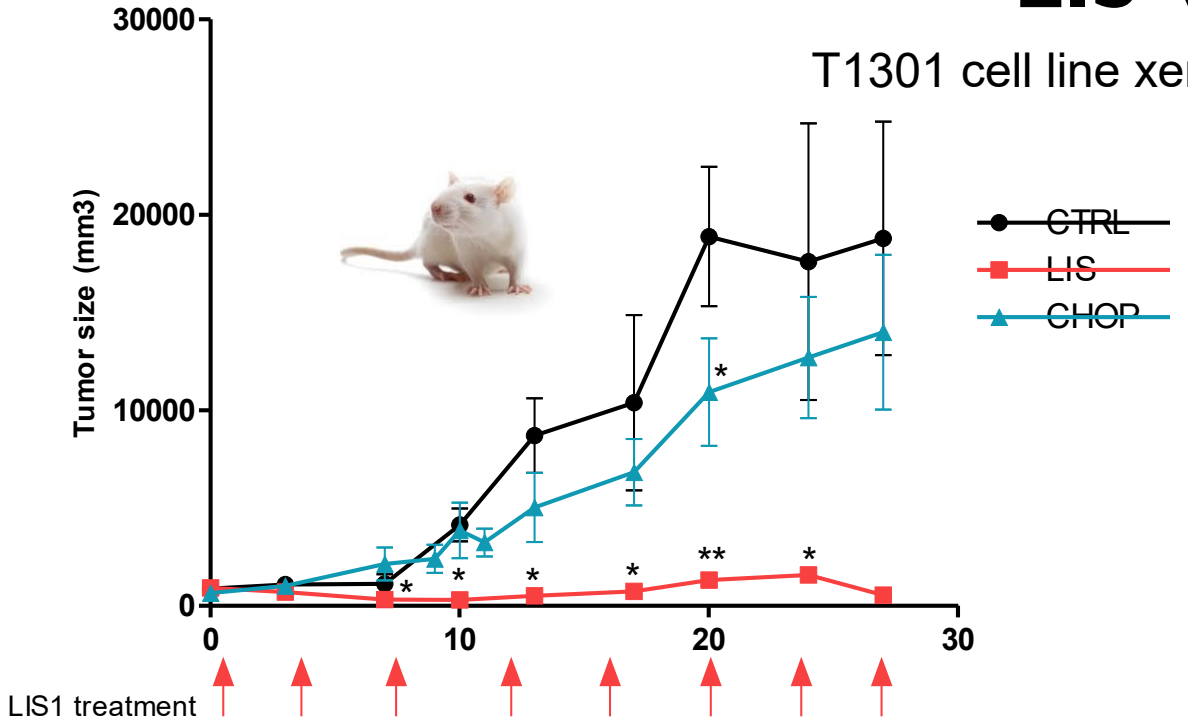


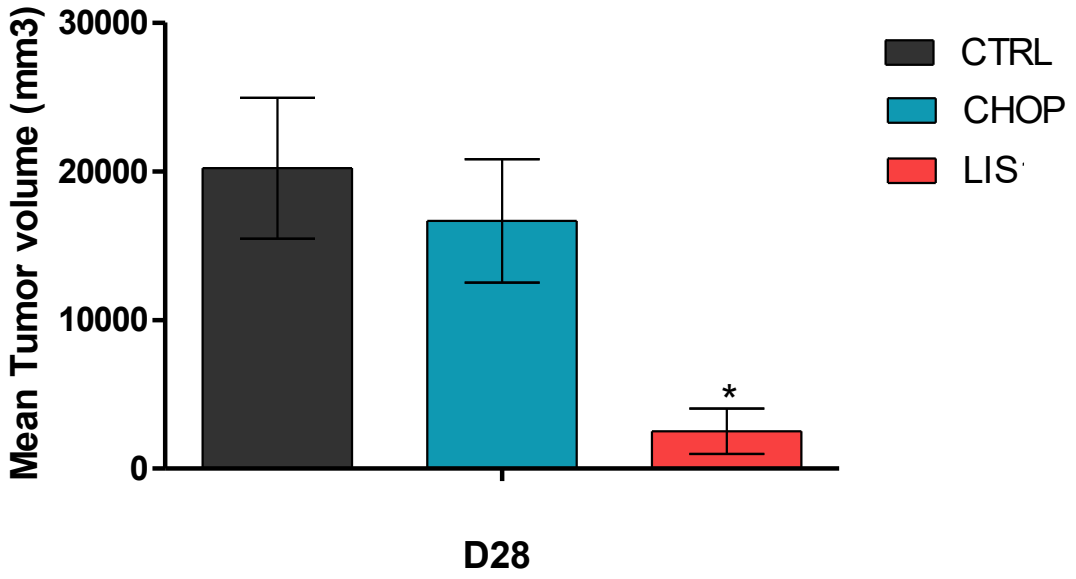
High potency of LIS22 against tumoral patient primary T cell tumors

In Vivo Antitumor Efficacy

In Vivo: LIS22 in Xenograft SRG rat model
LIS VS CHOP



*One way Anova – post Hoc test Fischer - *p<0.05, **p<0.01*



*One way Anova *p<0.01*

- **Treatments start when tumors reach 50-100mm^3, rat n=7**
- **LIS administration 40 mg/kg,** IP, twice a week for 4 weeks **- CHOP at highest tolerable dose :** 1 cycle = at D0 Cyclophosphamide 37,5 mg/kg, Doxorubicin 2,5 mg/kg and vincristin 0.07 mg/kg, at D0,D1,D2,D3,D4,D5 prednisolone 1.47 mg/kg

LIS showed superior efficacy and tolerance in SRG T1301 xenograft resistant to CHOP (PTCL SOC first line treatment)

Conclusion/Next Steps

LIS22 is multimodal polyclonal antibodies acting against T cell Lymphoma

LIS22 showed a specific antitumor activity with very low interaction with PBMC

LIS22 showed significantly in vitro and in vivo superior anticancer activity against T lymphoma compared to SOC

Next Steps

- LIS22 ODD granted in EMA and FDA In PTCL
- PALT1 Phase I/II, open-label, multi-center in relapsed/refractory peripheral T cells lymphoma (PTCL) patients, Inculsion started in July 2024 in France and Italy

Acknowledgement

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