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New Drugs & Ongoing Trials of PT/NKCLs in China

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Disclosures

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Yuqin Song, M.D., PhD

- Consultancy/advisory board participation (past 12 months):
  - AbbVie, BeiGene, AstraZeneca, MSD, Johnson & Johnson, Roche
- Research support (managed by institution):
  - Janssen, BeiGene, MSD, Takeda

- **Disease Burden & Routine Treatment in China**
- **New Drugs & Ongoing Trials in China**

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The Incidence of TCL

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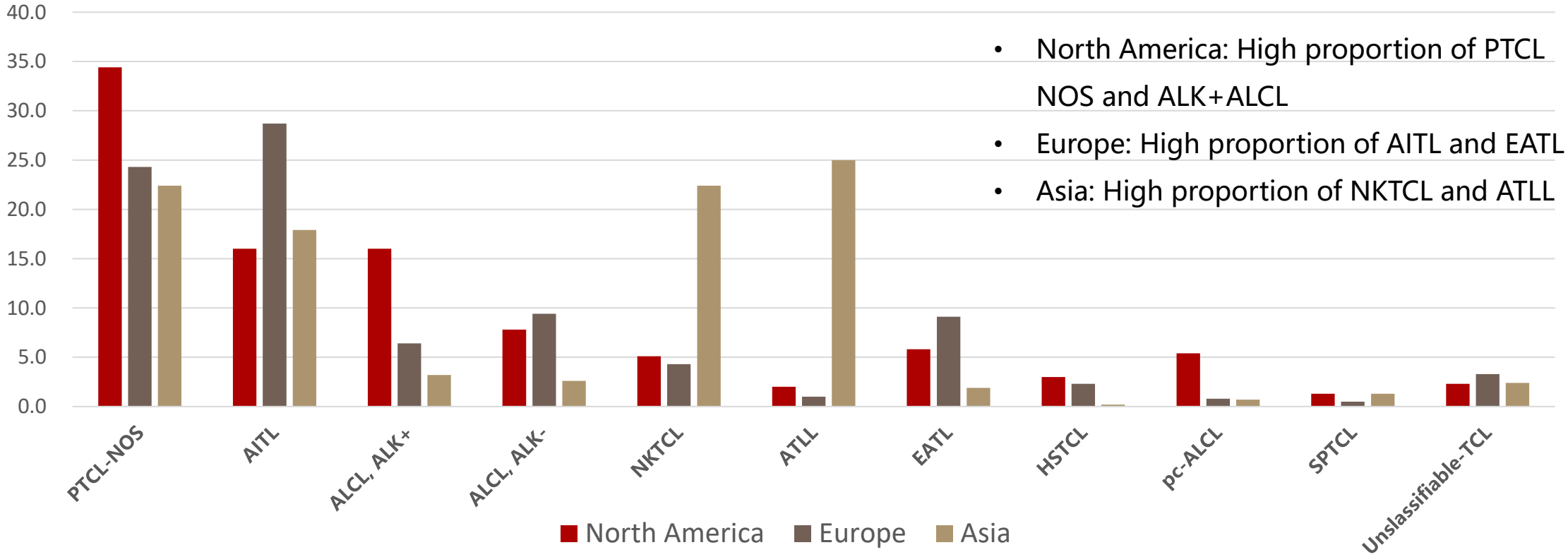
- **In Western countries: Mature T/NK lymphoma accounts for 15-20% of the incidence of aggressive lymphomas and 5-10% of the total lymphoma incidence;**
- **In China: Mature T/NK lymphoma accounts for 21% of the incidence among lymphoma patients.**



Julie V , James A , Dennis W . Journal of Clinical Oncology, 2008, 26(25):4124-30.
李小秋,李甘地,高子芬,等. 诊断学理论与实践, 2012, 11(2):5.

The Subtypes of Lymphoma in China

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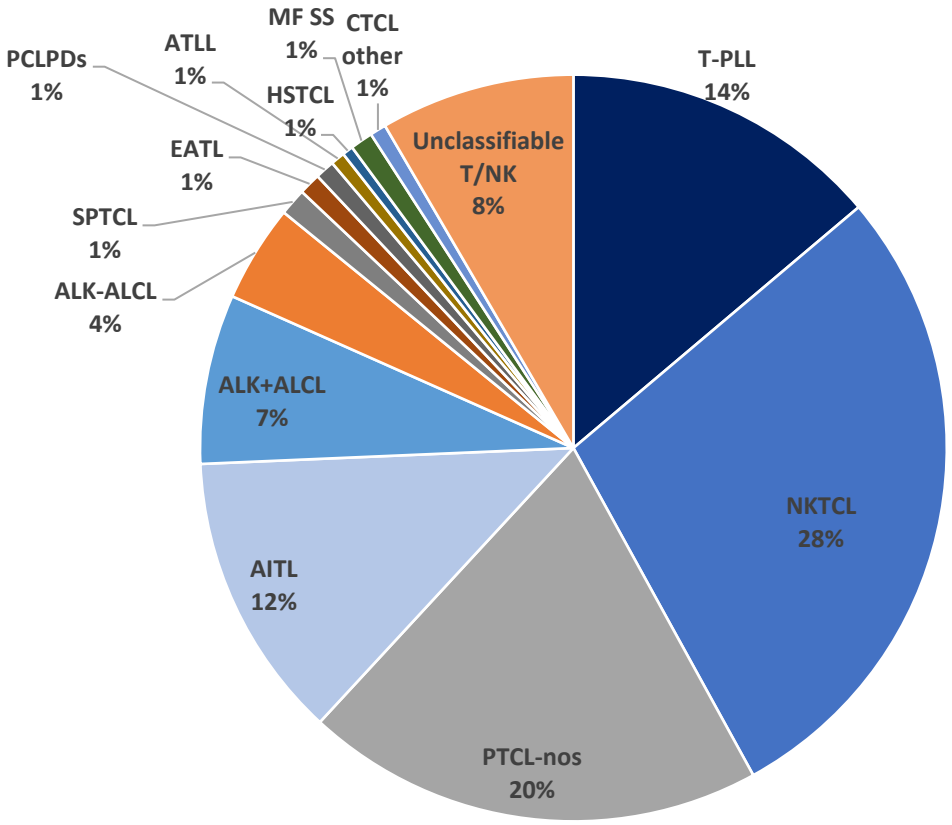
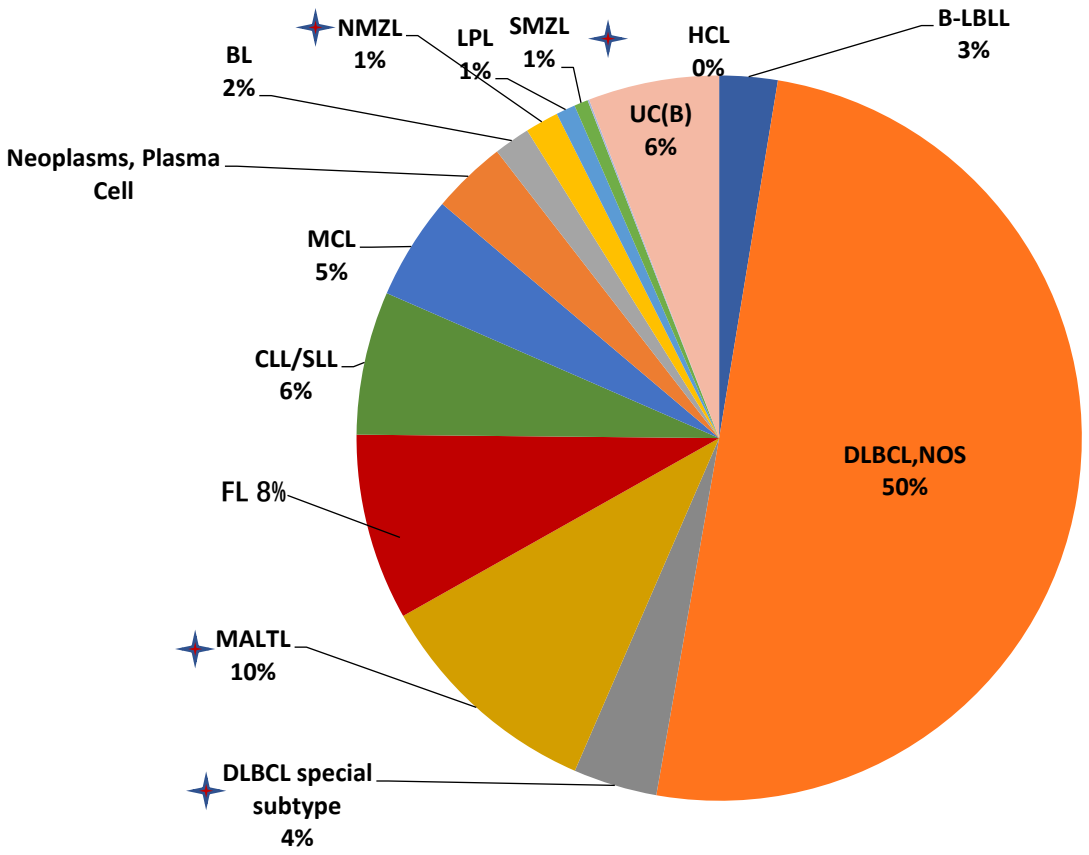
T/NKCL in China



BCL in China



Xiaoqiu Li, etc. 2012,11(2);, 111-115.

The Routine Treatment of PTCL

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Treatment naïve PTCL

1 Induction ⇨ CHOP+X (VP16, BV)

2 Consolidation for patients with poor prognosis ⇨ Auto or Allo-SCT

R/R TCL

3 Salvage ⇨ Chemotherapy

The aim of salvage treatment is to improve the efficiency and receive transplantation.

Prognosis of PTCL remains unfavorable

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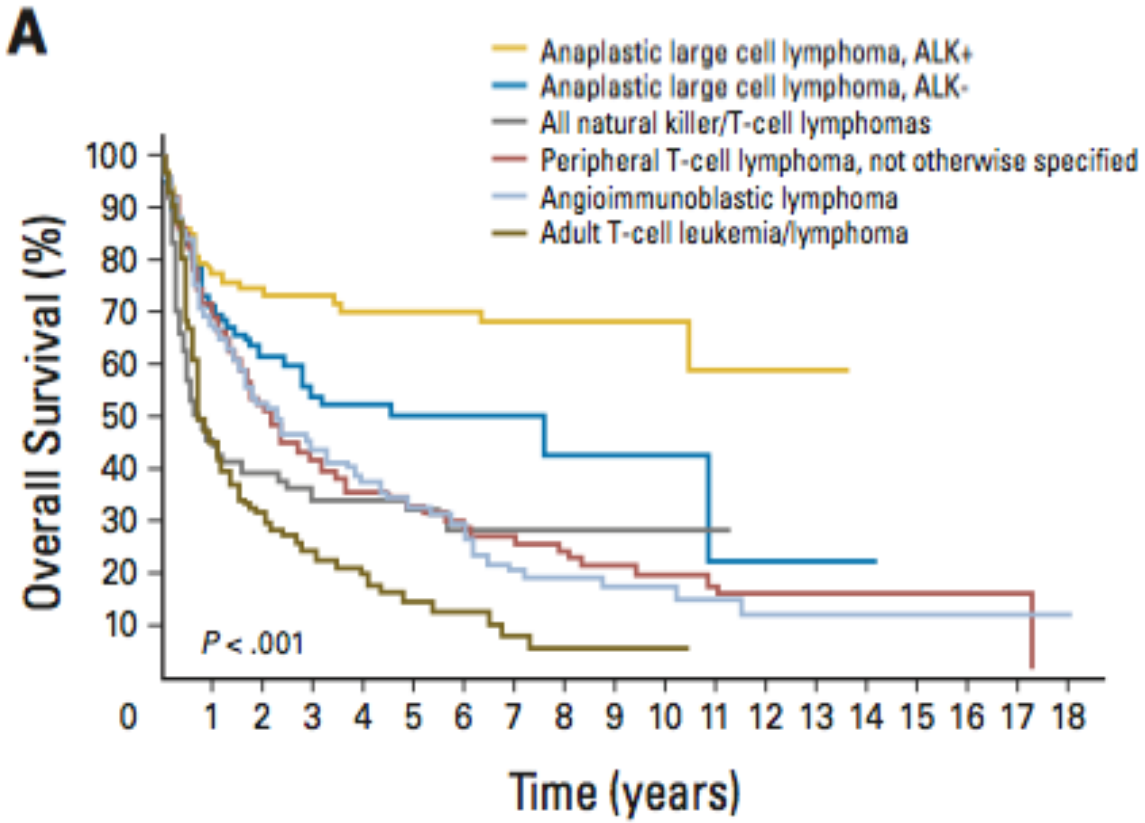
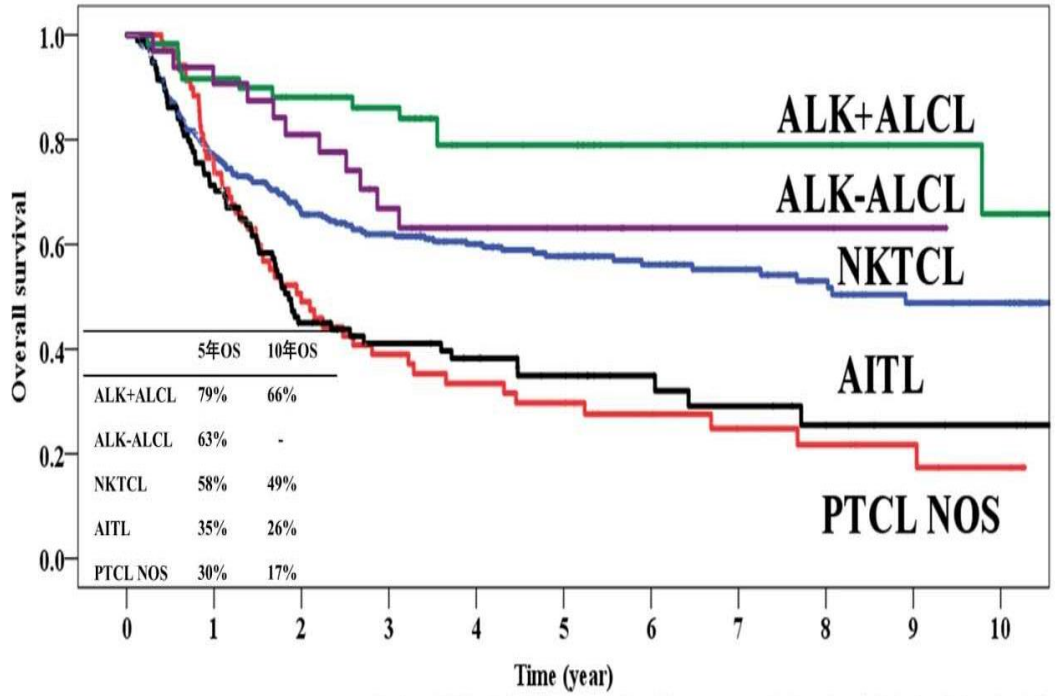
In Global



In Peking University Cancer Hospital

From 1996 to 2015



N=679, 5y-OS 50%，10y-OS 41%

Julie V , James A , Dennis W . Journal of Clinical Oncology, 2008, 26(25):4124-30.
Liu W, et al. Cancer Med, 2020.

The Survival of PTCL

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- With traditional treatment, the 5-year OS of most subtypes were not improved significantly over the past two decades, esp. AITL and PTCL-NOS.

	5-year overall survival (%)				
Category	**1996-2000**	**2001-2005**	**2006-2010**	**2011-2015**	***P* value**
PTCL (N = 679)	40.8	46.3	52.6	50.6	.592
ALK+ALCL (N = 60)	–	57.1	84.6	76.7	.750
ALK−ALCL (N = 34)	–	0	60	66.4	.481
NKTCL (N = 288)	–	61.6	59.7	53.0	.582
AITL (N = 94)	0	20.0	40.8	36.5	.021
PTCL NOS (N = 69)	50.0	25.0	21.8	33.8	.579
Others (N = 134)	37.0	30.1	41.7	37.5	.677

Liu W, et al. Cancer Med, 2020.

The Therapeutic Strategies of TCL

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Treatment naïve TCL

1 Induction ⇨ CHOP+**X** (VP16, BV, …?)

2 Consolidation ⇨ Auto or Allo-SCT

3* Maintenance ⇨ **X?**

R/R TCL

4 Salvage ⇨ Chemotherapy ± **X?**

The key to resolve poor prognosis of PTCL is to develop more effective novel drugs, even move to first-line treatment.

- Disease Burden & Routine Treatment in China
- **New Drugs & Ongoing Trials in China**

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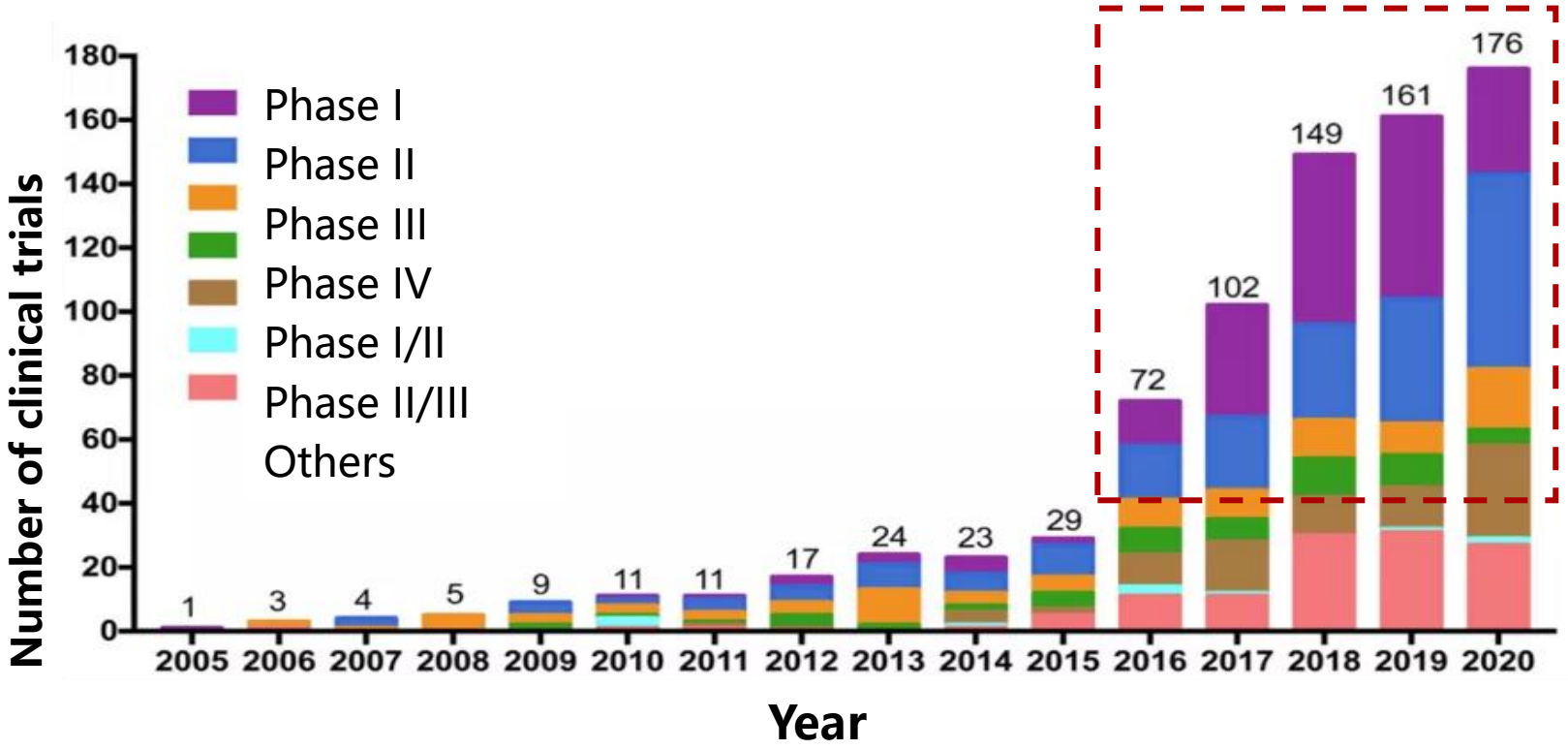
The number of lymphoma clinical trials in China



- The development of novel agents in lymphoma is quick since 2016.
- Phase I - II clinical trials showed a huge rise.
- The trends continued after COVID pandemic due to government encouragement.

The Lancet Regional Health - Western Pacific 2021; 8: 100097

From 2019 to 2024, 41 agents approved for marketing or new indications

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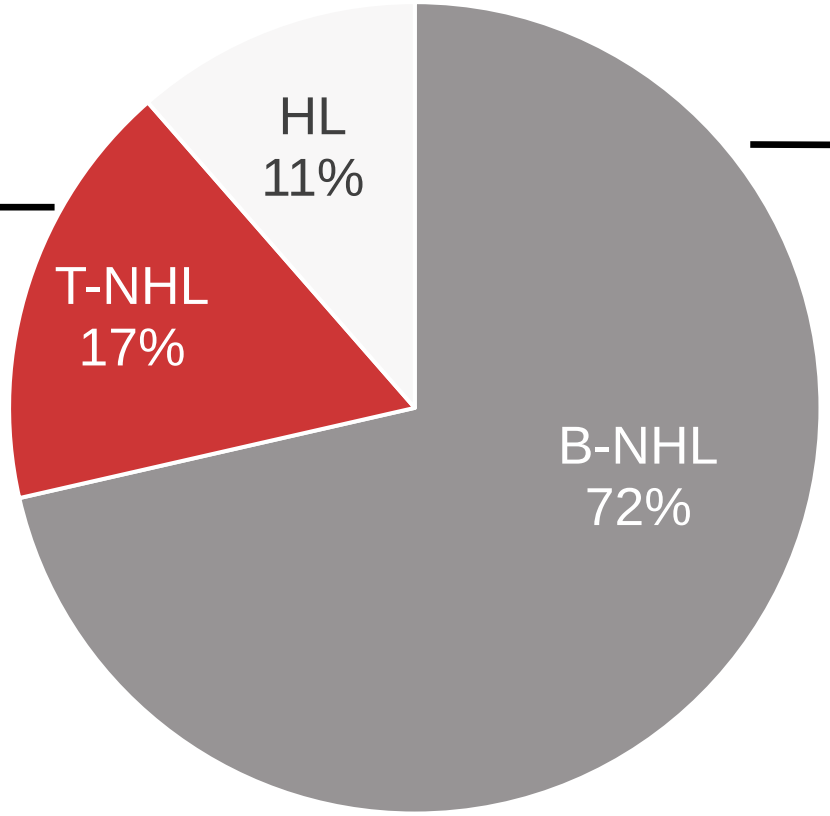
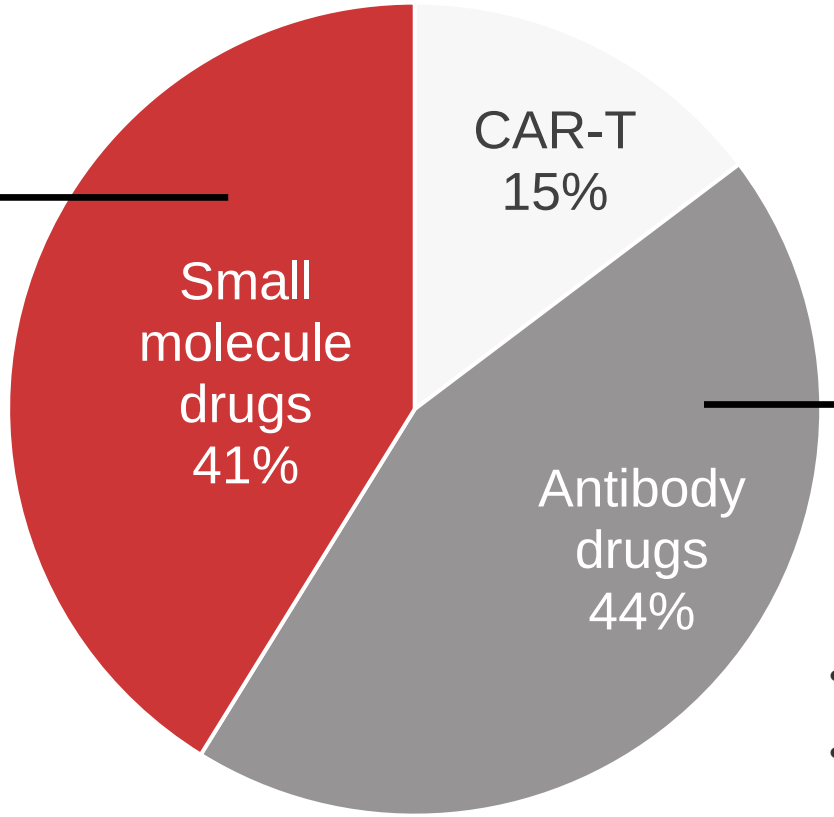
R/R PTCL

- Pralatrexate
- Brentuximab Vedotin
- Mitoxantrone hydrochloride liposome
- Golidocitinib
- Sugemalimab (R/R NKTCL)



- DLBCL 14.3%
- FL 17.1%
- MCL 14.3%
- MZL 2.9%
- Others 22.9%

cHL vs. B-NHL vs. T-NHL

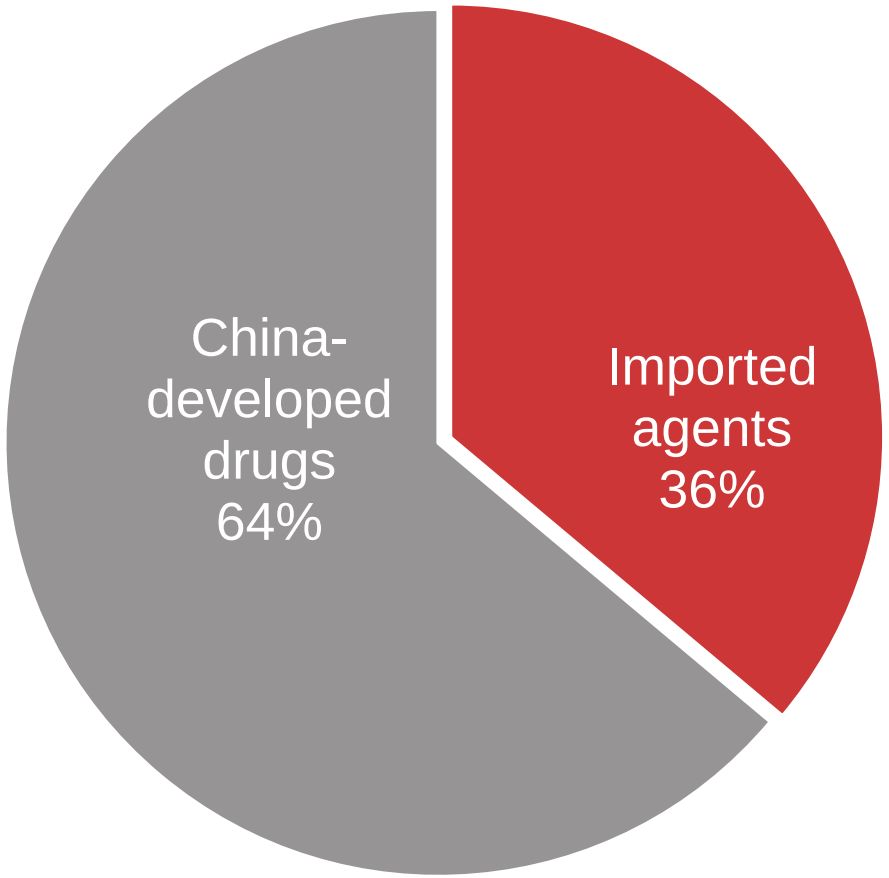


- JAK1 inhibitor 2.9%
- BTK inhibitor 20.6%
- PI3K inhibitor 8.8%
- Others 8.8%

- Anti-CD20 antibody 17.6%
- Anti-PD-1/L1 antibody 14.7%
- Bispecific antibody 2.9%
- Antibody–Drug Conjugates 8.8%

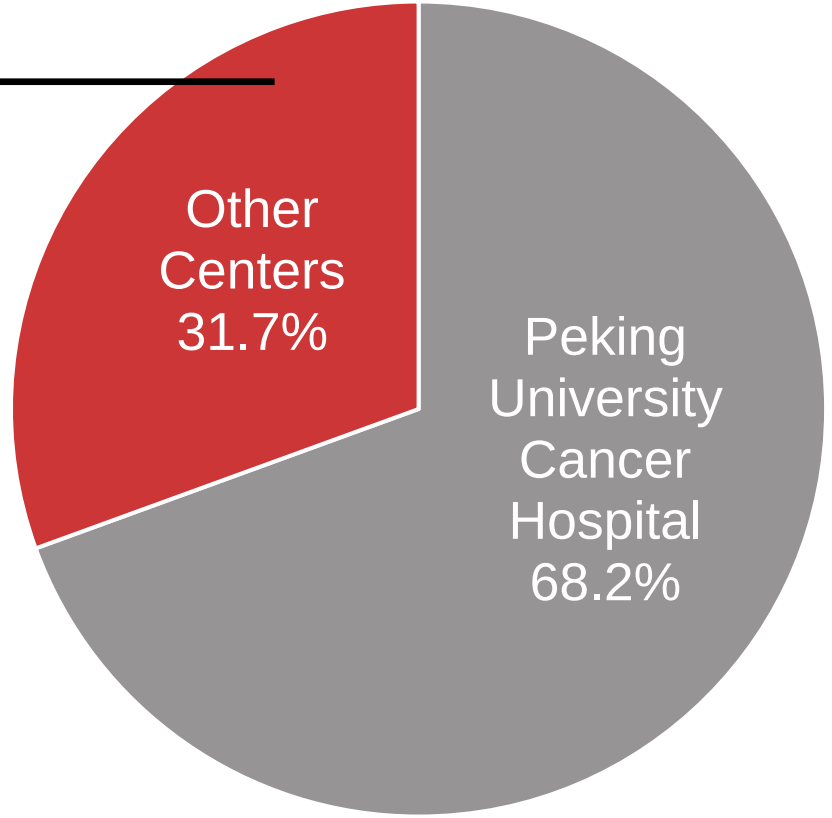
CAR-T vs. Antibodies vs. Small molecule drugs

Imported agents vs. China-developed agents



Peking University Cancer Hospital vs. Other Centers

- Shanghai Ruijin Hospital
- Sun Yat-sen University Cancer Center
- Cancer Hospital Chinese Academy of Medical Sciences
- Jiangsu Cancer Hospital
- Haematology Hospital Chinese Academy of Medical Sciences
- Others



Approval of new drugs or indications supported by Peking University Cancer Hospital

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2015	2017	2018	2019	2020	2021	2022	2023	2024
Chidamide	Ibrutinib	Plerixafor	Camrelizumab	Zanubrutinib Orelabrutinib Rituximab (Innovent)	Obinutuzumab Penpulimab	Mitoxantrone hydrochloride liposome injection Natulan/ Procarbazine Capsules	Polatuzumab vedotin Glofitamab	Golidocitinib Loncastuximab tesirine Pirtobrutinib
		Bortezomib	Tislelizumab	Lenalidomide (new indication) Pralatrexate Brentuximab vedotin	Zimberelimab Relma-cel (DLBCL)	Siltuximab (IL-6 mAb) Relma-cel (FL)	Acalabrutinib Orelabrutinib (MZL)	Relma-cel (MCL) Chidamide (DLBCL) Zanubrutinib (FL) Selinexor (DLBCL)

A series of clinical studies led by our department have successfully supported the approval of 31 new drugs or new indications for lymphoma in China.

New drugs or indications for PT/NKCL

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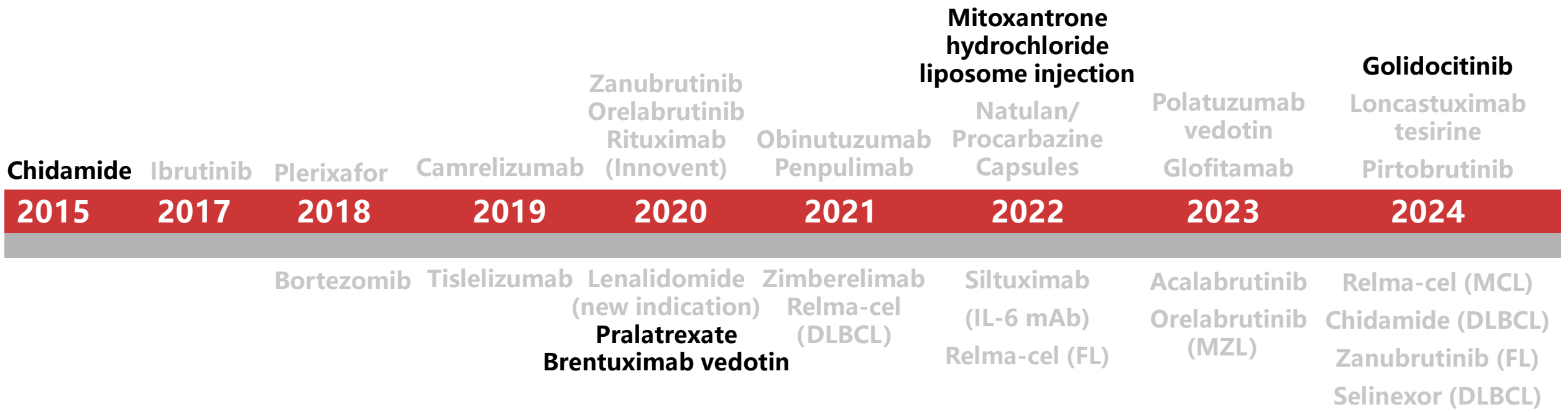
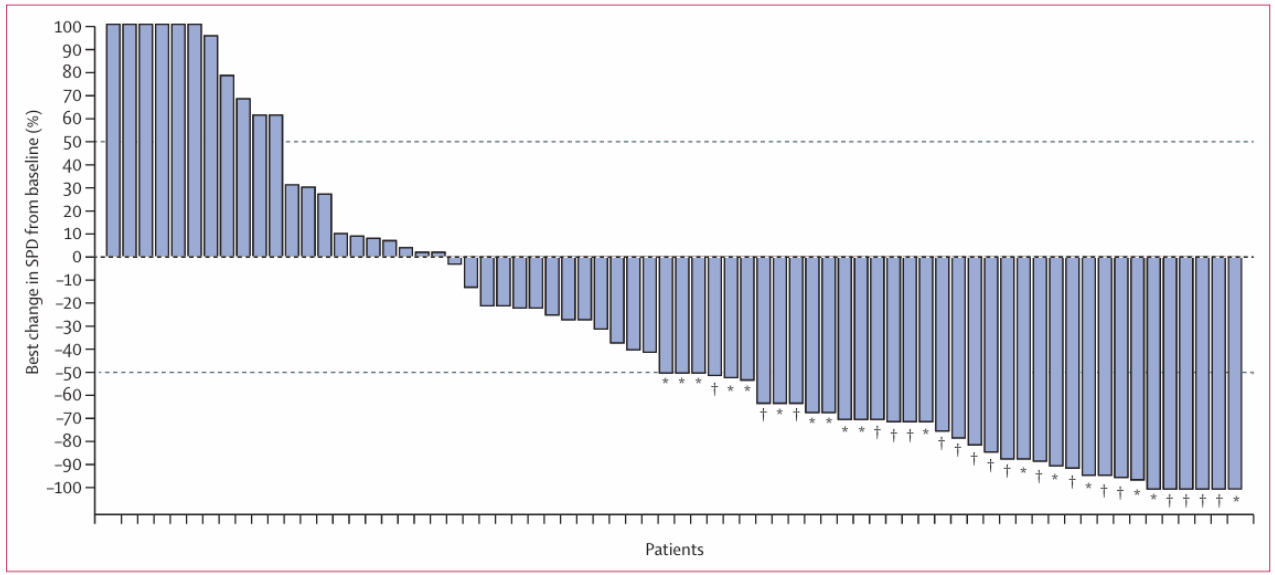


- Based bridging studies, to promote approvals of pralatrexate and BV in China.
- leading the phase I and pivotal phase II studies to promote approvals of Lipo-MIT and Golidocitinib in China.

JAK1i Golidocitinib in R/R PTCL

JAK1i Golidocitinib, the novel drug approved for R/R T cell lymphoma

- JACKPOT8 Part B: an open label, single arm, phase II, multicenter study
- 49 centers in Australia, China, South Korea, and the USA (Feb 26, 2021, and Oct 12, 2022)
- ORR 44.3%, CRR 23.9%, mFU: 12.5 months, mDOR: 20.7 months
- The most common grade 3-4 TRAEs were hematological toxicity



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Phase I dose escalation and expansion study of golidocitinib, a highly selective JAK1 inhibitor, in relapsed or refractory peripheral T-cell lymphomas

Y. Song[1], D. H. Yoon[2], H. Yang[3], J. Cao[4], D. Ji[4], Y. Koh[5], H. Jing[6], H. Eom[7], J. Kwak[8], W. Lee[9], J. Lee[10], H. Shin[11], J. Jin[12], M. Wang[13], Z. Yang[13], W. S. Kim[14]* & J. Zhu[1]*

Golidocitinib, a selective JAK1 tyrosine-kinase inhibitor, in patients with refractory or relapsed peripheral T-cell lymphoma (JACKPOT8 Part B): a single-arm, multinational, phase 2 study

Yuqin Song*, Luis Malpica*, Qingqing Cai, Weili Zhao, Keshu Zhou, Jianqiu Wu, Huilai Zhang, Neha Mehta-Shah, Kaiyang Ding, Yao Liu, Zengjun Li, Liling Zhang, Meifang Zheng, Jie Jin, Haiyan Yang, Yuerong Shuang, Dok Hyun Yoon, Sujun Gao, Wenyu Li, Zhimin Zhai, Liqun Zou, Yaming Xi, Youngil Koh, Fei Li, Miles Prince, Hui Zhou, Lie Lin, Hui Liu, Pamela Allen, Fernando Roncolato, Zhenfan Yang, Won-Seog Kim*, Jun Zhu

ClinicalTrials.gov, NCT04105010
Yuqin Song et al. 2023 ASH: Oral 305.
Yuqin Song et al. Lancet Oncol 2024; 25: 117–25

JAK1i Golidocitinib in R/R PTCL

Histology Subtypes[1]	Total Number of Subjects, n[2] (%)	ORR[3], n (%)	CRR[3], n (%)
PTCL, NOS	50 (56.8)	23 (46.0)	14 (28.0)
AITL	16 (18.2)	9 (56.3)	4 (25.0)
ALCL	10 (11.4)	1 (10.0)	0
NKTCL	3 (3.4)	2 (66.7)	1 (33.3)
Others	9 (10.2)	4 (44.4)	2 (22.2)

Data cut-off date: February 16, 2023

- Golidocitinib demonstrated anti-tumor efficacies across most PTCL subtypes, esp. AITL and PTCL-NOS
- Due to its favourable benefit–risk profile in patients with R/R PT/NKCL, and most patients from China, it was approved in China in 2024.

[1] The diagnosis of histological subtypes was based on central pathology review.
[2] The percentage of subjects in each subtype was calculated based on the total number of efficacy analysis set (n = 88) as the denominator.
[3] The ORR and CRR were calculated based on total number of subjects as the denominator. Tumor response was assessed by IRC per Lugano 2014 criteria.

ClinicalTrials.gov, NCT04105010
Yuqin Song et al. 2023 ASH: Oral 305.
Yuqin Song et al. Lancet Oncol 2024; 25: 117–25

SHR2554, first EZH2 inhibitor in R/R PTCL

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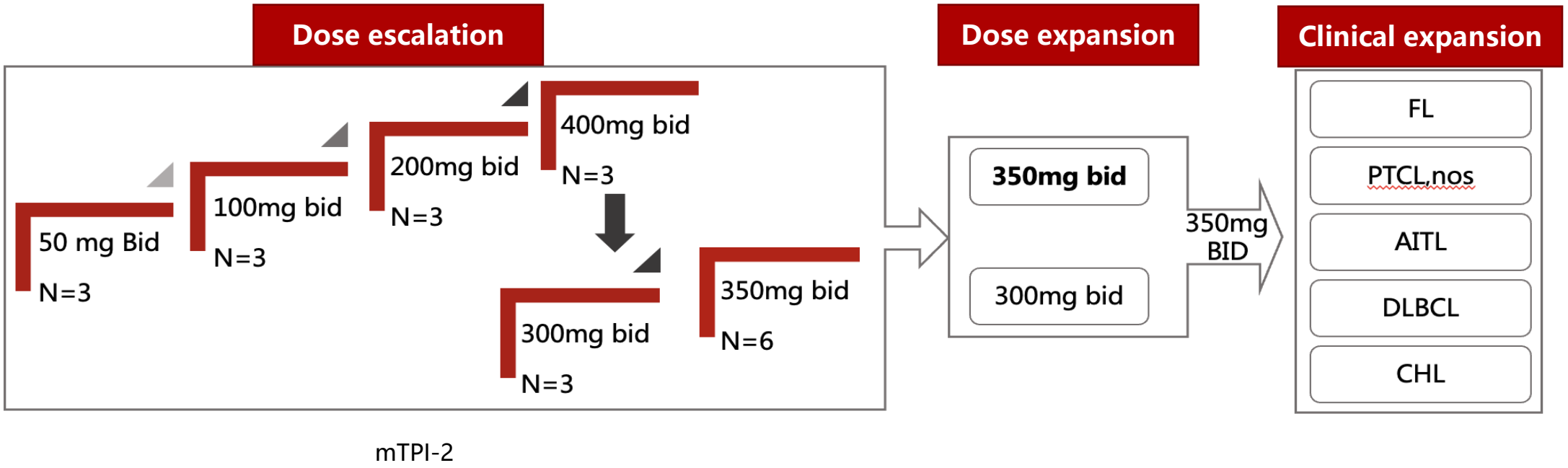
a first-in-human, dose-escalation, dose-expansion, and clinical expansion phase 1 trial



ClinicalTrials.gov, NCT03603951,

1. Song Y, et al. Lancet Haematol 2022; 9: e493–503

EZH2 inhibitor SHR2554 in R/R PTCL

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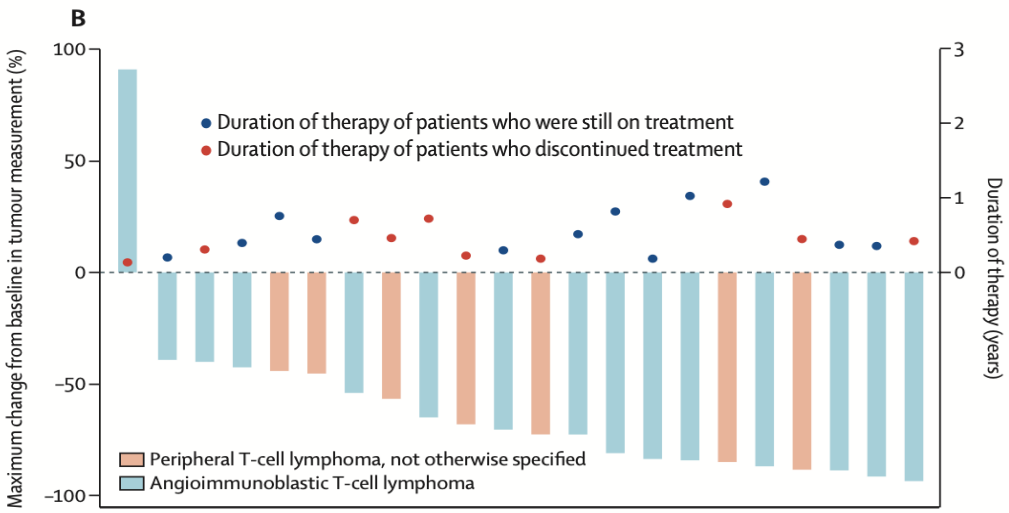
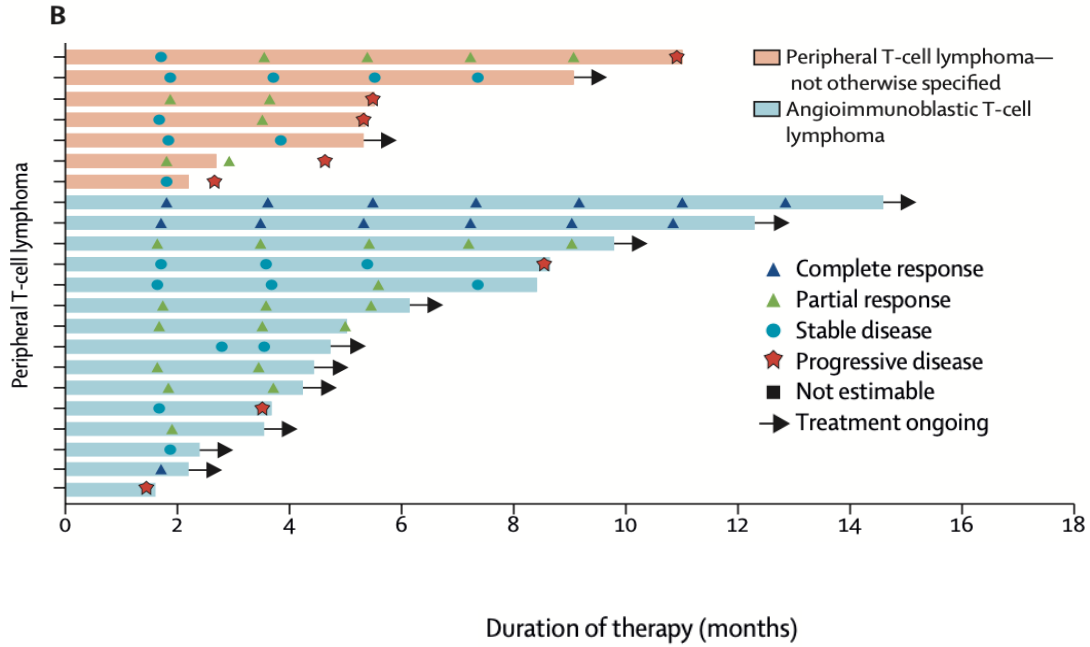
A multicenter phase 1 study in 13 hospitals

- 113 patients with r/r mature lymphoid neoplasms: **28** (25%) **PTCL**
- ORR: 64%(14/22); median duration of response 7.4months; AITL 67%, PTCL-NOS 57%



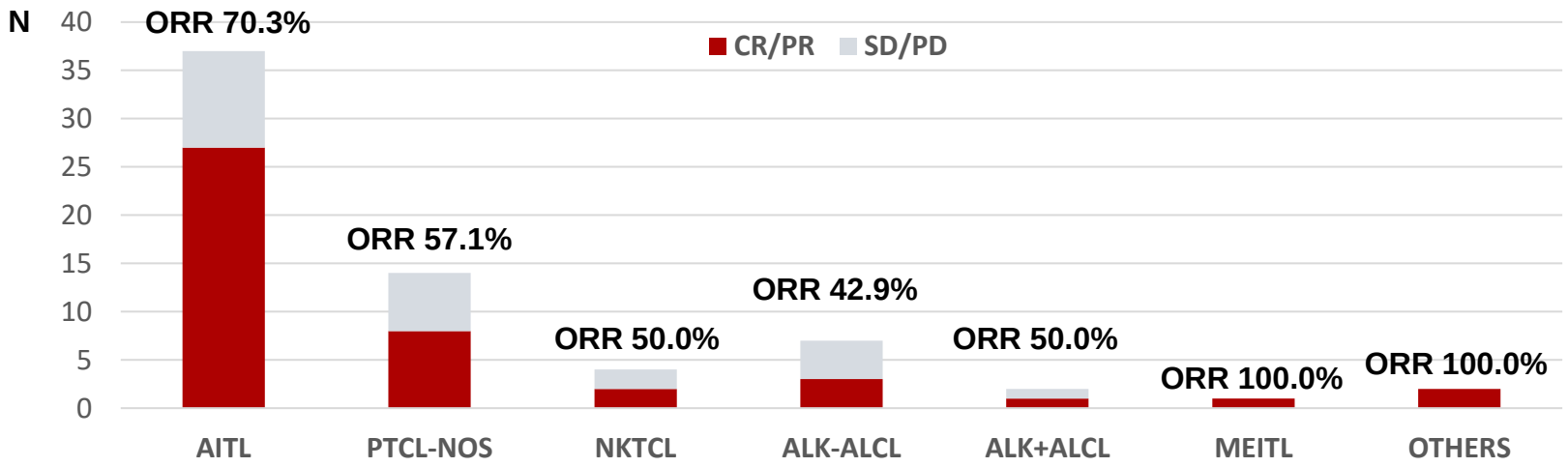


ClinicalTrials.gov, NCT03603951,

1. Song Y, et al. Lancet Haematol 2022; 9: e493–503

EZH2 inhibitor SHR2554 in R/R PTCL

- Given its favourable safety profile and promising anti-tumor activity in R/R PTCL, we selected R/R PTCL as the first indication in pivotal phase II trials.
- As of Dec 20, 2024, N=67, IRC-assessed ORR 64.2%, CRR 32.8%, mPFS 10m, mOS 16.9m

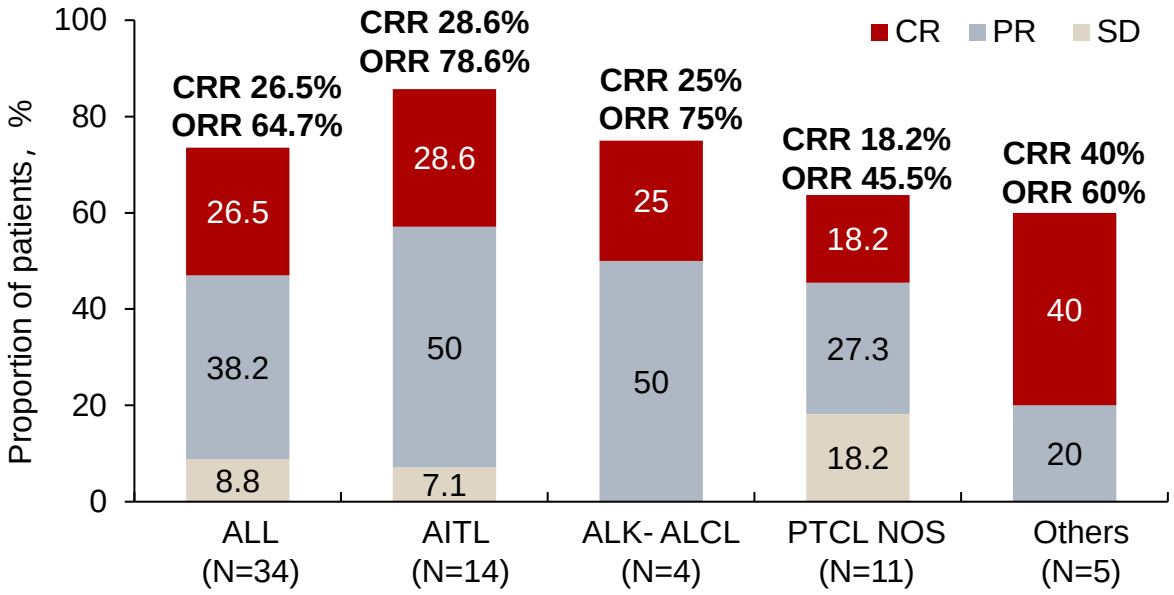


- Responses were still ongoing in 51.2% (22/43) of the responders, and the estimated mDoR was 18.7 months
- The indication for R/R PT/NKCL is waiting for approval this year.

https://library.ehaweb.org/eha/2025/eha2025-congress/4159323

EZH1/2i HH2853 in R/R PTCL

BOR	ALL (N=34)	300mg (N=15)	400mg (N=16)	600mg (N=3)
CR，%	26.5	26.7	25.0	33.3
PR，%	38.2	33.3	43.8	33.3
SD，%	8.8	13.3	6.3	0
PD，%	23.5	26.7	18.8	33.3
ORR，% [95% CI]	64.7 [46.5, 80.3]	60.0 [32.3, 83.7]	68.8 [41.3, 89.0]	66.7 [9.4, 99.2]
DCR，% [95% CI]	73.5 [55.6, 87.1]	73.3 [44.9, 92.2]	75.0 [47.6, 92.7]	66.7 [9.4, 99.2]
mTTR，m [95% CI]	1.87 [1.7, 5.6]	1.84 [1.7, 3.7]	1.91 [1.7, 5.5]	4.63 [3.7, 5.6]



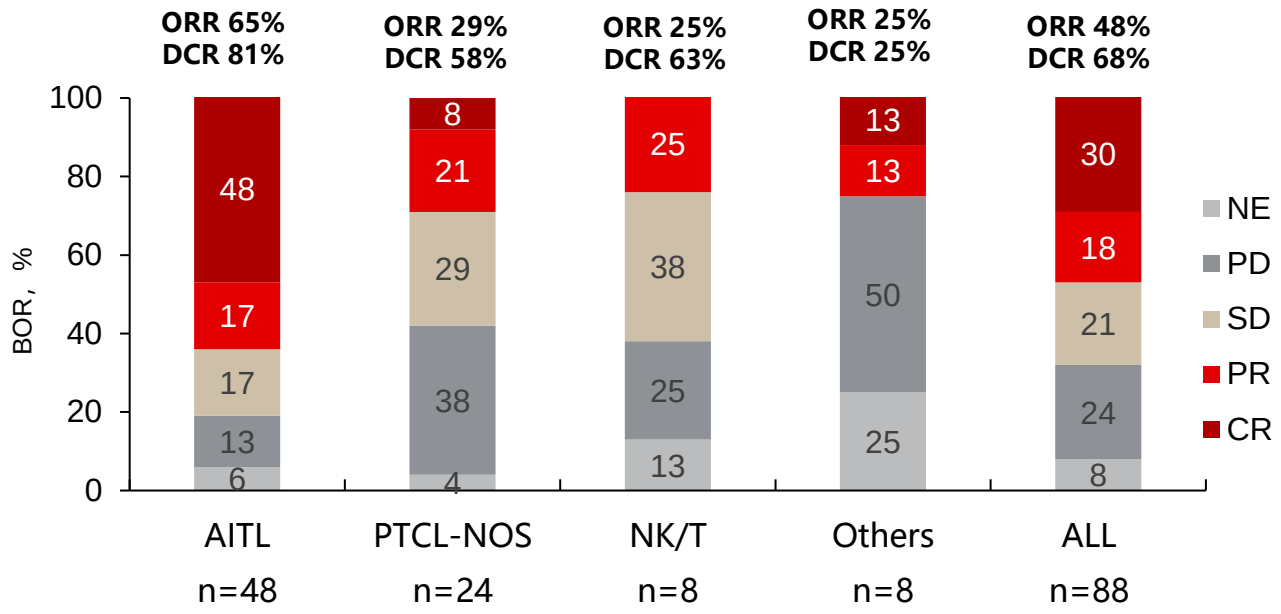
- HH2853 has significant and durable efficacy in the treatment of R/R PTCL.
- The ORR 64.7%, and the CRR 26.5%. The ORR and CR of AITL are the highest.
- After a median follow-up of 4.6 months, the mDOR, mPFS, and mOS have not been reached.

Hong HM, et al. 2023 ASH abstract 304.

PI3Kδi Linperlisib in R/R PTCL

- A multicenter phase 2 study in China from 25 sites

- ORR 48%; CR 30%; DCR 68%
- mFU 13.9 months: mDOR NR; mPFS 5.5m; mOS 14.2m
- Responses were demonstrated across almost all subtypes
- well-tolerated safety profile



✓ This clinical trial provides a new option for patients with R/R PTCL. Linperlisib is waiting for approval in this year.

CTR20210333

Yuqin Song et al. 2023 ASH: Oral 306.

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Exploring CHOP+X in treatment naïve PTCL

CHOP+X in treatment naïve PTCL

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A Phase Ib/III, Open-label, Multi-center Study of SHR2554 With CHOP/CHOEP in Treatment-naïve Patients With Peripheral T-cell Lymphoma (IND study)

- **Regimen: CHOP/CHOPE + SHR2554** vs. CHOP/CHOPE+ placebo
- Inclusion Criteria:
  - ✓ Males or females aged 18-70 years (inclusive);
  - ✓ Histologically confirmed peripheral T-cell lymphoma;
  - ✓ ECOG PS score of 0 or 1;
  - ✓ Life expectancy ≥ 12 weeks;
  - ✓ Have measurable lesions ;
  - ✓ The subject is willing and able to comply with the visit schedule, dosing schedule, laboratory tests, and other clinical study procedures.

NCT06173999

CHOP+X in treatment naïve PTCL

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- **A single-arm, multicenter phase II study in treatment naïve nTFHL (IIT study)**
- **Regimen: CHOP+linperlisib (80 mg oral QD) ×6cs → autoSCT → linperlisib monotherapy maintenance for 1 year**
- Inclusion criteria:
  - ✓ histologically confirmed nTFHL (Nodal T-follicular helper cell lymphomas)
  - ✓ Age 18-65 years
  - ✓ scheduled for autologous HSCT
- **As of July 8, 2024, N=15, with 14 patients evaluable for efficacy:**
  - ✓ mFU 85 days, **ORR 100% (14/14), CRR 78.6%**, median time to CR was 43.5 days
  - ✓ Grade ≥3 TRAEs were reported in six patients (40%), mainly Hematological toxicity.
- Linperlisib combined with CHOP shows promising efficacy and manageable safety in newly diagnosed nTFHL patients. This study is ongoing.

Weiping Liu, Yao Liu, Zengjun Li, et al. Blood 2024; 144 (Supplement 1): 6389.

CHOP+X in treatment naïve PTCL

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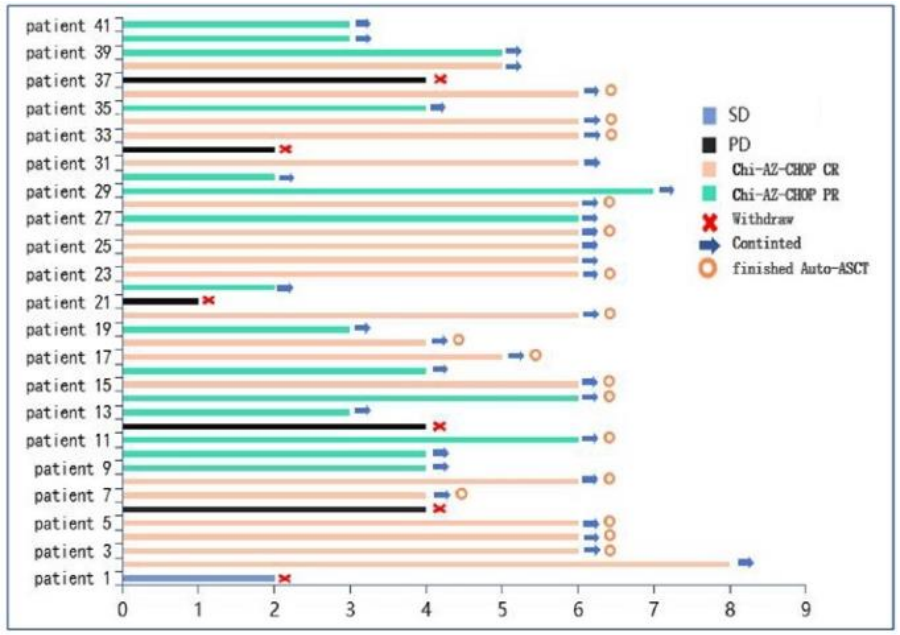
Phase II study of chidamide combined with azacitidine and CHOP followed by transplantation in the treatment of newly diagnosed PTCL (IIT study)



Efficacy:

- As of December 2023, 41 patients received Chi+AZ-CHOP treatment for at least 2 cycles, with a median treatment time of 5 cycles
- All: ORR 85.3%, CRR 48.7%
- For AITL (N=23): ORR 86.9%, CRR 60.8%
- 17 patients received ASCT, after ASCT, the ORR was 100%, and the CRR was 88.2%

Safety:

- ≥G3 Hematological AE: Neutropenia (52.9%), FN (35.4%), anemia (28.4%), and thrombocytopenia (25.7%).
- ≥G3 Non-Hematological AE: Hypokalemia (27.1%), nausea (36.8%), vomiting (25.2%), and fatigue (36.5%).
- No treatment-related deaths have been reported.

Chunyan Xiao. et al. 2024 EHA Poster 2106

Conclusion

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- Undergoing routine treatment, the prognosis of most PT/NKCL were still poor, esp. patients in R/R setting.
- The survival of patients receiving transplantation is relative better, but in the real world, only 16% patients can eligible for transplantation.
- The development of novel drugs is growing quickly in China in past 10 years.
- Even with the approvals of some novel agents in R/R PTNKCL in China, there are still significant unmet clinical needs, esp. moving to first-line therapy.

I would like to thank all patients and their family, investigators and team members!

Thanks